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VERRUCA PLANA AND EPITHELIAL NEVUS

INCLUDING A STUDY OF EPIDERMODYSPLASIA VERRUCIFORMIS

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Our interest in verruca plana and epithelial nevus was prompted by the observation that the vacuolar alterations of epidermal cells in both of these conditions suggested a possibly common pathologic anomaly. We were impressed particularly by the morphologic relations of verruca plana and epidermodysplasia verruciformis, and, in fact, this investigation was undertaken when we had the opportunity recently to examine patients suffering from epidermodysplasia verruciformis at the Mayo Clinic and sought to distinguish histologically between this disease and verruca plana, which it grossly simulates. Also, one of us (H. M.) [1] has recognized for many years the fact that apparently related epidermal abnormalities occur in some forms of linear nevus. It was the purpose of this study to determine whether the epidermal lesion in verruca plana is the same as the lesion in certain forms of epithelial nevus and also to appraise the nosologic status of epidermodysplasia verruciformis, which has been variously classified by different authors among verrucae, precancerous dermatoses and nevoid disturbances of the skin.

VERRUCA PLANA

In the literature there are comparatively few detailed reports of histologic studies of verruca plana. Thin's pioneer histologic description is fragmentary.[2] The tendency long has been to cite the early observa-

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1. Montgomery, H., in discussion on Finnerud.[29]

2. Thin, G.: An Unusual Case of Warty Growths on the Face, Med.-Chir. Tr. London **46**:283-288, 1881.

tion of Darier [3] in his single case: that in verruca plana all layers of the epidermis are thickened, especially the granular and prickle cell layers, and that no alteration is visible in the cells of the prickle cell layer. Dubreuilh [4] erroneously recorded the same structure. Among the first to mention the characteristic vacuolated cells in verruca plana was Lupis.[5] Martinotti [6] described vacuolar changes in the epidermis, scarcity of normal keratohyalin and parakeratosis, but neither the cellular change nor the distribution of keratohyalin is clearly represented in his illustrations. Kyrle [7] observed that epithelial cells in the deeper layers of the rete as well as in the vicinity of the stratum corneum occasionally appeared to be degenerated, with the cytoplasm swollen and often, also, the nucleus. The paucity of reports on verruca plana is, however, no indication that the histologic structure of the disease is not familiar to dermatopathologists, as shown, for example, by the paper of Becker,[8] whose photomicrograph illustrates the characteristic alterations. Lewandowsky and Lutz,[9] Fuchs,[10] Hopf [11] and others have also briefly described the structure of the plane wart.

Certain clinical features of verruca plana will now be enumerated, to indicate how close may be its likeness to lesions of epidermodysplasia verruciformis. The color may range from yellowish brown to brownish red or even violet, the yellow hue predominating among younger patients. The size of the warts varies. Larger lesions consist of tiny pinhead-sized papules grouped together, forming either a smooth papule or a mosaic pattern close inspection of which discloses the identity of the individual lesions. The top can be scraped off with a curet, and a smooth, moist or slightly bleeding base remains, on which the verruca usually recurs promptly. Important to recognize, because of similar

3. Darier, J.: Verrues planes juvéniles de la face, Ann. de dermat. et syph. **19**:617-622 (Oct. 25) 1888.

4. Dubreuilh, W.: Des hyperkératoses circonscrites, Ann. de dermat. et syph. **27**:1158-1204, 1896.

5. Lupis, G.: Contribuzione allo studio della verrucca giovanile, Gior. d. mal. ven. **32**:451-462, 1897.

6. Martinotti, L.: Ricerche sulle anomalie e le alterazione del processo della carneifiazione nei principali stati morbosi della cute umana, Gior. d. mal. ven. **64**: 758, 1923.

7. Kyrle, J.: Vorlesungen über Histo-Biologie der menschlichen Haut und ihrer Erkrankungen, Berlin, Julius Springer, 1925, vol. 1, pp. 153-158.

8. Becker, S. W.: The Pigmentary Form of Verruca Plana, Arch. Dermat. & Syph. **34**:265-267 (Aug.) 1936.

9. Lewandowsky, F., and Lutz, W.: Ein Fall einer bisher nicht beschriebenen Hauterkrankung (Epidermodysplasia verruciformis), Arch. f. Dermat. u. Syph. **141**:193-203, 1922.

10. Fuchs, H.: Ein Fall von eigenartiger Dyskeratose (Epidermodysplasia verruciformis), Arch. f. Dermat. u. Syph. **141**:225-231, 1922.

11. Hopf, G.: Ueber eine bisher nicht beschriebene disseminierte Keratose (Akrokeratosis verruciformis), Dermat. Ztschr. **60**:227-250 (Feb.) 1931.

lesions in epidermodysplasia verruciformis, is the pigmentary, ephelis-like form of verruca plana described by Becker.[8]

That warts of this type occur most commonly on the face and hands is well known, as are also their infectiousness and their tendency to occur in linear distribution after a scratch. Often verruca vulgaris is associated. (A flattened form of verruca vulgaris is sometimes

Fig. 1.—Verruca plana lesions of one year's duration on the wrist and forearm of a woman 43 years old.

observed which superficially simulates verruca plana but histologically can be distinguished.) Patients who have verruca plana may be children or adults—younger persons predominating—and the duration of the disease in instances in which it is refractory may be a decade or longer [12] (fig. 1).

12. (*a*) Herxheimer, K., and Marx, K.: Zur Kenntnis der Verrucae planae juveniles, München. med. Wchnschr. **41**:591-594 (July 24) 1894. (*b*) Djamdjieff, G.: Des verrues planes juvéniles, Arch. clin. de Bordeaux **6**:468-490, 1897.

Histologic Picture of Verruca Plana.—The following histologic aspects of verruca plana are drawn from a study of specimens removed by us for biopsy (fig. 2). The papule, which is sharply defined, presents an increase in all layers of the epidermis. The stratum corneum is hyperkeratotic, in loose lamellas or in a loosely felted "basket weave" pattern. Just above the granular layer a parakeratotic zone is sometimes encountered, and occasionally a spotted or patchy distribution of flattened nucleated cells can be observed.

Among the cells of the granular layer vacuolar alterations are constantly present; these may extend to a depth of half the thickness of the rete malpighii. Here many cells are enlarged up to two or three times their normal size. The cytoplasm is clear or converted into a fine-skeined reticulum or consists merely of a few trabeculated strands extending from the wall of the cell to the nucleus. The nuclei, pale and granular, lie centrally or peripherally within the cells. Pyknotic nuclei were hardly to be found in our sections. Keratohyalin granules, in fine particles or in coarse clumps, are present only in relation to the cytoplasm and are not deposited free within the clear spaces; nor do all the altered cells necessarily show a deposit of keratohyalin. The walls of the cells are thickened and closely apposed, so that epithelial bridges usually are not visible. The vacuolar changes occur in isolated cells or, more commonly, in groups or islands of cells. The modified granular layer is prominent in some lesions and relatively slight in others. Nuclear inclusions have not been recognized in our material, in which there was at least one specimen from an early lesion.

The prickle cell layer is moderately acanthotic, with elongation of the rete ridges. The layer of basal cells shows no abnormality; only a sparse sprinkling of pigment is present. In some cases a slight perivascular infiltrate of lymphocytes occurs in the upper part of the cutis.

Histologic Distinction Between Verruca Plana and Verruca Vulgaris.—The lesions of verruca vulgaris differ from those of verruca plana, and the variation is more than one of degree, notwithstanding the opinion of Kühnemann [13] and some subsequent writers. Characteristic for verruca vulgaris [14] are acanthosis and hyperkeratosis, with proliferating epithelial ridges penetrating into the cutis, more deeply at the center than peripherally, the papillary bodies thereby appearing to be

13. Kühnemann, G.: Contributions to the Anatomy and Histology of Verruca Vulgaris, Brit. J. Dermat. **1**:328-338 (Aug.); 366-378 (Sept.) 1889.

14. Gans, O.: Histologie der Hautkrankheiten. Die Gewebsveränderungen in der kranken Haut unter Berücks ihrer Entstehung und ihres Ablaufs, Berlin, Julius Springer, 1927, vol. 2, pp. 117-121.

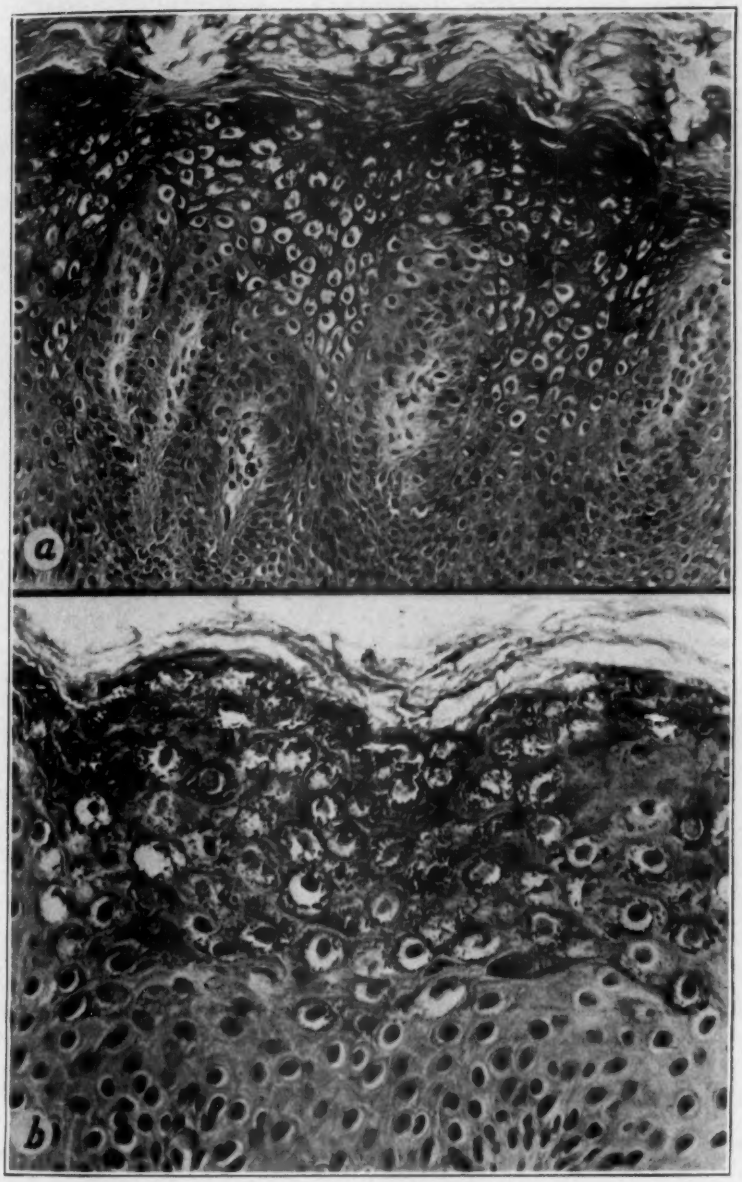

Fig. 2.—Verruca plana. *a*, section from a lesion of three years' duration on the wrist of a woman aged 20; note the loosely felted hyperkeratosis, narrow zone of parakeratosis, acanthosis, increased thickness of stratum granulosum and pronounced vacuolation of epidermal cells (hematoxylin and eosin, × 165). *b*, section of a lesion of six months' duration from a child's forehead, showing details of vacuolation of epidermal cells and increase in granular layer distribution of keratohyalin (hematoxylin and eosin, × 320).

directed radially from the center (fig. 3). Large vacuolated cells are observed both in the prickle cell layer and in the stratum granulosum. The nuclei, folded, shriveled or pyknotic and sometimes multiple, are surrounded by a perinuclear clear halo and a peripheral foamy zone of cytoplasm. The region of degenerated cells is more scattered and is less regular than in verruca plana. These vacuolar changes are characteristic but are probably not pathognomonic for verruca.

An unusual type of parakeratosis occurs in the horny layer,[15] marked by (1) intermittent tiers of retained nuclei, usually in the suprapapillary

Fig. 3.—Verruca vulgaris. Typical lesion from the thumb, showing extreme hyperkeratosis, a peculiar type of spotted parakeratosis and marked acanthosis and papillomatosis and vacuolar degenerative changes in the stratum granulosum (hematoxylin and eosin, [*a*] × 35 and [*b*] × 90).

regions, and (2) dispersed swollen cells, in the cytoplasm of which vacuoles appear. In the latter cells the nucleus increases in size with the formation of homogeneous, amphophilic or basophilic inclusion bodies. In late stages of verruca vulgaris the nuclear inclusions become

15. Lipschütz, B.: Zur Kenntnis der Ätiologie und der strukturellen Architektonik der Warze (Verruca vulgaris), Arch. f. Dermat. u. Syph. **148**:201-217, 1924.

sparse or disappear entirely. We have not observed them in our sections of verruca plana.

Homogeneous acidophilic, round, oval, crescentic and irregular intracellular masses are sometimes found in verruca vulgaris. The product of a degenerative change ("keratohyalinoid degeneration"), they probably have nothing in common with the specific nuclear inclusions.

EPIDERMODYSPLASIA VERRUCIFORMIS

Epidermodysplasia verruciformis, described by Lewandowsky and Lutz [9] in 1922, recently has been the subject of two reports in the American literature, by Sullivan and Ellis [16] and Wise and Satenstein.[17] The disease has been considered to be an epithelial nevus, a hereditary type of dystrophy with a precancerous tendency, or an extensive form of verruca. In some cases there is a history of parental consanguinity. It appears in generalized or restricted forms, usually during the early life of the patient, although it has been known not to manifest itself until after middle age. Epidermodysplasia verruciformis is a verrucose dermatosis, comprised of numerous flat-topped, warty and lichenoid lesions, rounded or polygonal, closely resembling the papules of verruca plana. The lesions may be grayish, dull pink, red, violet or brown; they are of irregular size, varying from that of a pinhead to that of a pea or larger, and by their tendency to become confluent they sometimes form large plaques. They appear in groups and as isolated papules, as a rule asymptomatically. Ephelis-like lesions have been reported. The eruption is distributed most profusely on the face, neck and extremities, usually in a symmetric pattern, being most prominent on the dorsa of the hands and feet. Mucosal lesions were described in the case of Hoffmann [18] on the vermilion border of the lip and in the case of Louste, Lévy-Franckel, Cailliau and Schwartz [19] in the urethra. Sunlight in some instances has been incriminated as a factor predisposing to the distribution of lesions on the exposed parts. In certain cases isolated lesions have undergone epitheliomatous degeneration of the basal or squamous cell type.

At the Mayo Clinic we have observed 4 patients who had epidermodysplasia verruciformis (figs. 4 and 5). Two patients had the localized

16. Sullivan, M., and Ellis, F. A.: Epidermodysplasia Verruciformis, Arch. Dermat. & Syph. **40**:422-432 (Sept.) 1939.

17. Wise, F., and Satenstein, D. L.: Epidermodysplasia Verruciformis (Lewandowsky-Lutz), Arch. Dermat. & Syph. **40**:742-753 (Nov.) 1939.

18. Hoffmann, E.: Ueber verallgemeinerte Warzenerkrankung (Verrucosis generalisata) und ihre Beziehung zur Epidermodysplasia verruciformis (Lewandowsky), Dermat. Ztschr. **48**:241-266, 1926.

19. Louste; Lévy-Franckel, A.; Cailliau, and Schwartz: Epidermodysplasie verruciforme avec lésions papillomateuses de la muqueuse uréthrale, Bull. Soc. franç. de dermat. et syph. **41**:270-279 (Feb.) 1934.

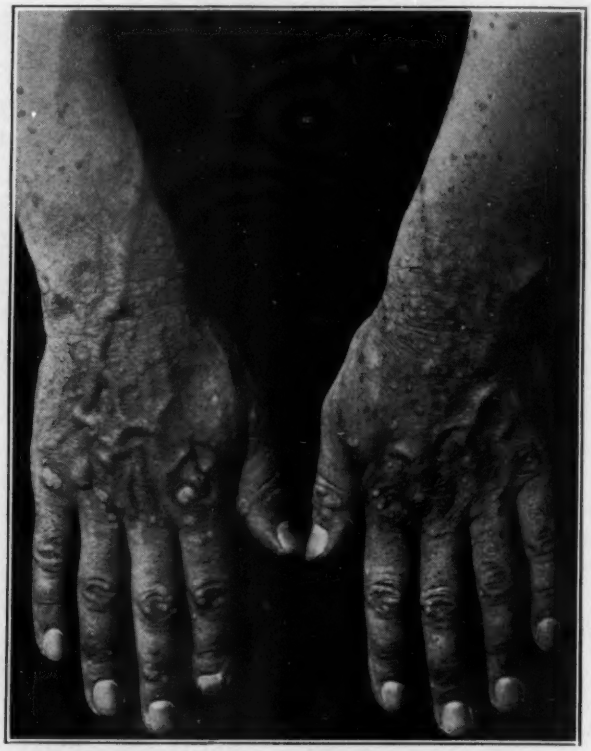

Fig. 4.—Epidermodysplasia verruciformis affecting a man aged 37. The lesions had been present since early childhood. Similar lesions were situated on the neck and face.

Fig. 5.—Epidermodysplasia verruciformis of many years' duration. The lesions are localized on the hands. An epithelioma was removed from one hand.

form (on the dorsa of the hands). One of them exhibited also a small crusted squamous cell epithelioma on the back of the left hand, which had been present for two years. As in Hoffmann's case, the histologic characteristics of this lesion suggested origin from preexisting senile keratosis, however, rather than from one of the verrucous papules.

Histologic Picture of Epidermodysplasia Verruciformis.—In biopsy of lesions from our patients the following features have been distinguished: The papule is slightly elevated and sharply demarcated from the adjacent portions of skin. Salient in the pathologic process are hyperkeratosis and acanthosis of the epidermis, in the rete cells of which appears a pronounced and unusual vacuolation. The laminas of the stratum corneum usually are loosely interwoven, and in 1 case a zone of nuclear retention was visible.

Vacuolation may be perceived in cells of the rete only a few layers removed from the intact basal layer. The earliest expression of this vacuolar change is the appearance of a clear perinuclear zone, with a corresponding enlargement of the cell. As the process advances, the nuclear chromatin becomes coarsened, and often the nucleus becomes pyknotic, crescentic and pushed eccentrically toward the periphery of the cell. Epithelial bridges cannot be demonstrated between cells severely swollen and closely packed against each other, but they are visible in the early stages. These swollen, clear cells may compose a large portion of the prickle cell layer (figs. 6 and 7).

The cellular alteration seems to attain its height in the stratum granulosum, which may reach three or four times normal thickness. Here the vacuolation is accentuated by the distribution of keratohyalin, which occurs only within the peripheral pale, scanty, foamy cytoplasm, in the form of angular clumps, filaments and fine granules. Not all of the cells participate in the modification described, for scattered normally developed cells appear adjacent to swollen ones. Likewise, the changes are not uniform at any one level; deeper cells may show more advanced degeneration than superficial (and therefore older) cells. We found no abnormal numbers of mitotic figures, nor were inclusion bodies demonstrated in nucleus or cytoplasm. A paucity of pigment was noted in the basal cells.

The cutis evidenced no significant variation aside from an occasional slight infiltration of lymphocytes about some of the blood vessels.

Pathogenesis of Epidermodysplasia Verruciformis.—The succession of changes which take place in the epithelial cells have been analyzed step by step by Kogoj.[20] Much discussion prevails in the literature

20. Kogoj, F.: Die Epidermodysplasia verruciformis, Acta dermat.-venereol. 7:170-179, 1926.

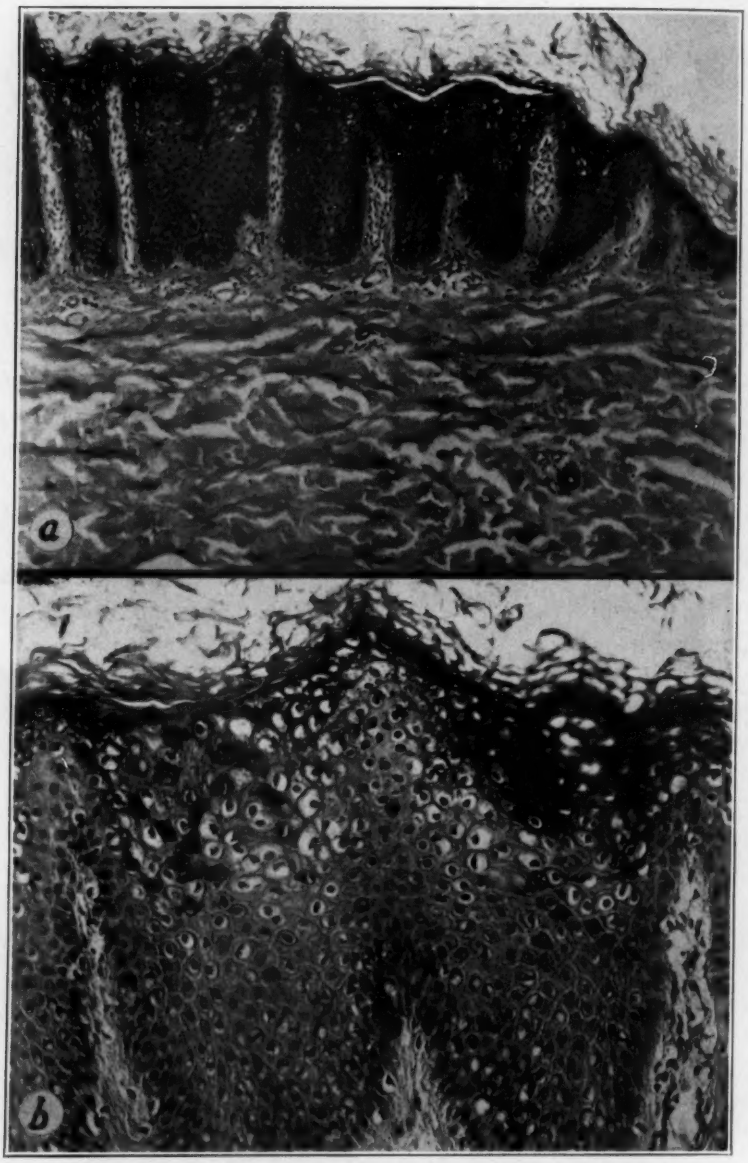

Fig. 6.—Epidermodysplasia verruciformis: sections from patient in figure 4. *a*, loose hyperkeratosis, increase in granular layer, vacuolation of cells, acanthosis and papillomatosis (hematoxylin and eosin, × 75). *b*, details of vacuolar changes and pyknosis of nuclei (hematoxylin and eosin, × 175).

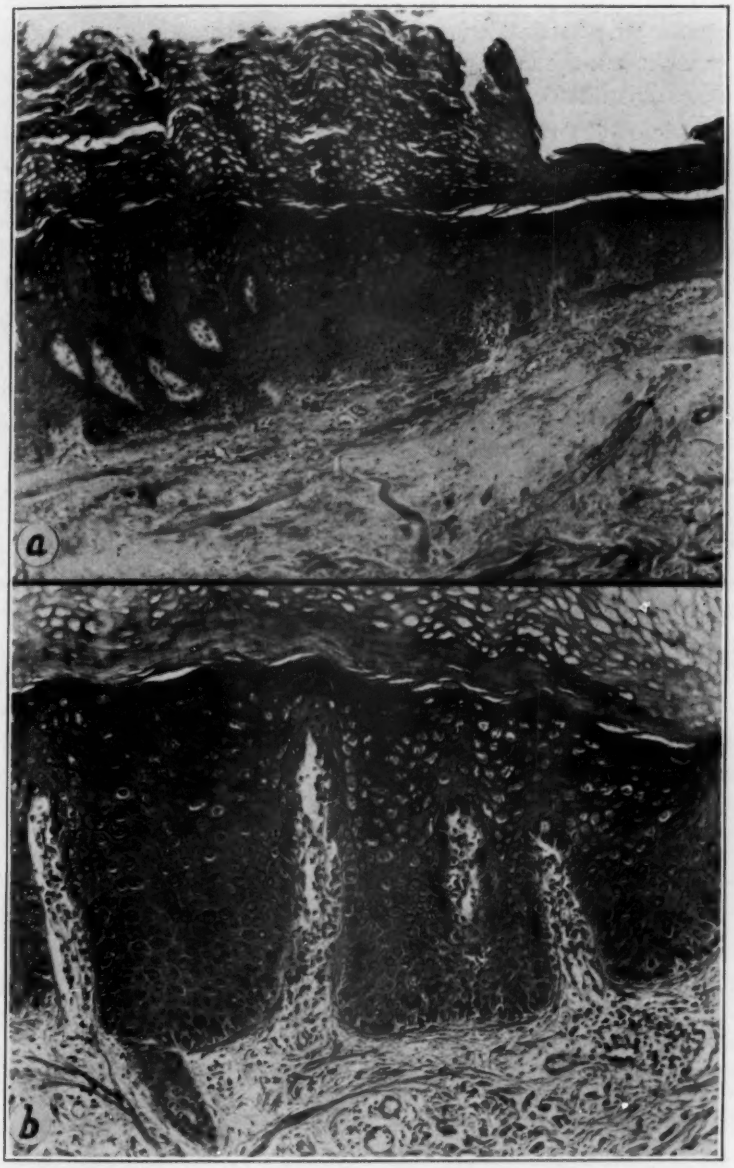

Fig. 7.—Epidermodysplasia verruciformis. *a*, section from patient in figure 5; note basket-weave-like arrangement of edematous stratum corneum (hematoxylin and eosin, × 65). *b*, section from the back of the hand of a man aged 39, who also had cancer of the penis. The lesions limited to the hands were present throughout life. Note the histologic resemblance to verruca plana (hematoxylin and eosin, × 100).

concerning the essential nature of the cellular disintegration in the epidermis. At first glance it may suggest an eczematous edema; but negating this possibility are the absence of intercellular edema (spongiosis) and multiloculated vesicles and the paucity of inflammatory reactions in the cutis.

More difficult to exclude is the suggestion that epidermodysplasia verruciformis represents a form of dyskeratosis. One of us (H. M.) [21] has emphasized the distinction between benign types of dyskeratosis, such as are seen in Darier's disease, and malignant types of dyskeratosis, such as are seen in Bowen's disease and in precancerous dermatosis. It may be worthy of note that vacuolar changes in the epidermal cells constitute one of the dyskeratotic features found almost regularly in keratoses and epitheliomas induced by arsenic and also found frequently in Bowen's disease.[22] An essential aspect of dyskeratosis, however, whether it is benign or malignant, is keratinization of individual cells—a feature lacking in our histologic material. Louste and his associates [19] characterized the process in epidermodysplasia verruciformis as a disturbance of keratinization in which the cell failed to achieve dyskeratosis in its evolution (as in Darier's disease) but underwent a change to a state of vacuolation, with or without a nucleus. In our opinion, Darier's disease has little resemblance, either clinically or histologically, to epidermodysplasia verruciformis. Maschkilleisson [23] regarded epidermodysplasia verruciformis as a dysplasia akin to Darier's concept of dyskeratosis. He could find no other condition in which vacuolation, in the sense of "clear degeneration," occurred so extensively in the epidermis, and he classed the disease as genodermatosis, related not only to the cutaneous dystrophies but also to the group of precancerous dermatoses, especially Bowen's disease. Civatte [24] placed epidermodysplasia verruciformis among the precancerous eruptions. That in some cases the condition may not be far removed from the classification of dyskeratotic dermatoses becomes evident on study of the clinically

21. Montgomery, H.: Precancerous Dermatosis and Epithelioma in Situ, Arch. Dermat. & Syph. **39**:387-408 (March) 1939.

22. Montgomery, H.: Arsenic as an Etiologic Agent in Certain Types of Epithelioma: Differential Diagnosis from, and Further Studies Regarding, Superficial Epitheliomatosis and Bowen's Disease, Arch. Dermat. & Syph. **32**:218-233 (Aug.) 1935.

23. Maschkilleisson, L. N.: Ist die Epidermodysplasia verruciformis (Lewandowsky-Lutz) eine selbständige Dermatose? Ihre Beziehungen zur Verrucositas, Dermat. Wchnschr. **92**:569-578 (April 18) 1931.

24. Civatte, A.: IV. Érythro-kératodermies naeviques précancéreuses; épidermodysplasie verruciforme, in Darier, J.; Sabouraud, R.; Gougerot, H.; Milian, G.; Pautrier, L. M.; Ravaut, P.; Sézary, A., and Simon, C.: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 6, pp. 685-692.

similar condition described by Sézary and Lévy-Coblentz,[25] in which, however, the histologic changes make for segregation of the disease in this case from epidermodysplasia verruciformis. Our review of the case reported by Sullivan and Ellis,[16] including inspection of slides, leads us to concur in their opinion regarding the dyskeratotic and malignant changes present. If one were to judge purely on the basis of the histologic changes, the condition in their case could fit in with the dyskeratotic group of diseases. It is probable that when more material has been studied these two categories will be more clearly defined.

Another possibility with regard to the pathogenesis of the cellular vacuolation is that the process is a manifestation of a nevoid state. Wise and Satenstein[17] favored this explanation, particularly in view of their finding of clear cells in the basal layer of the lesions as well as in the clinically normal skin. (Our own observations and perusal of other cases in the literature indicate, however, that vacuolation of the unaffected skin is an exceptional circumstance and not a common feature.) The relation of the epidermal lesions in epidermodysplasia verruciformis to those in clearly defined epithelial nevus will be considered later.

Finally, the question of whether the changes encountered histologically in epidermodysplasia verruciformis are not similar to those found in verruca plana has been mentioned by a number of authors and has impressed us frequently in the course of this investigation. In the following section we shall examine this apparent relation in detail.

THE QUESTION OF RELATION BETWEEN EPIDERMODYSPLASIA VERRUCIFORMIS AND VERRUCA PLANA

A considerable discussion in the literature on epidermodysplasia verruciformis centers around the possibility that the dermatosis is simply a generalized or disseminated form of verruca. Hoffmann[18] and Kogoj[20] independently advanced the concept of a lymphogenous or hematogenous dissemination of verruca virus. To these authors the histologic structure of epidermodysplasia verruciformis did not differ significantly from that of the wart. Gans[14] accepted epidermodysplasia verruciformis as being probably an extensive form of plane or ordinary wart occurring on predisposed skin, as have also other writers.[26]

Among published comments on the relation between epidermodysplasia verruciformis and verruca plana, the following reports may

25. Sézary, A., and Lévy-Coblentz, G.: Naevi verruciformes, Bull. Soc. franç. de dermat. et syph. **40**:220-223, 1933.

26. (*a*) Glaubersohn, S. A.: Contribution à l'étude de la verrucose généralisée (epidermoplasia verruciformis), Ann. de dermat. et syph. **9**:378-387 (May) 1928. (*b*) Wendlberger, J.: Zur Frage der "Epidermodysplasia verruciformis," Arch. f. Dermat. u. Syph. **179**:707-716, 1939. (*c*) Santalov, N.: Zur Kasuistik der Verrucae disseminatae, abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **29**:74, 1929.

be cited: Lewandowsky and Lutz [9] were aware that many of the papules in epidermodysplasia verruciformis simulated plane warts and that swelling of the epithelial cells was observed in plane and ordinary warts. The same points of similarity were brought out also by Fuchs,[10] who, commenting on the hydropic cells, asserted that they are certainly to be found in verruca plana but that there was no recorded instance of such cells dominating the picture so strikingly. Hidaka [27] compared the vacuolation in epidermodysplasia verruciformis with that in verruca plana and concluded that there were differences between the two processes. Kogoj enumerated conditions in which vacuolation of epithelial cells occurred and cited Lipschütz to the effect that hydropic degeneration was not necessarily a specific change of warts. Maschkilleisson,[23] on the other hand, stated that in his sections of verruca plana none of the characteristics of epidermodysplasia verruciformis were detected; the warts exhibited hypertrophy of all layers of the epidermis, sometimes with intracellular edema, but the latter feature was not outstanding. Wendlberger [26b] was unable to determine, from the histologic appearances alone, "where verrucosis stops and epidermodysplasia verruciformis begins." Freudenthal and Spitzer [28] agreed that warts may be widely distributed and that the disorder of the cells characteristic for epidermodysplasia verruciformis occurs in other dermatoses also, although uncommonly. They were convinced that many cases have been reported as instances of epidermodysplasia verruciformis in which, because they lack criteria established by Lewandowsky and Lutz, one might question whether disseminated verruca was not the correct diagnosis. Wise and Satenstein [17] recognized that the histologic picture in their sections of an early lesion resembled the structure of the flat juvenile wart, as did also Louste and his associates.[19] Of pertinent interest is the expression of opinion with regard to the case presented by Finnerud,[29] in which, to one of us (H. M.), were exhibited histologic changes suggesting epithelial nevus (the clinical picture thereby fitting the localized form of epidermodysplasia verruciformis), but which Obermayer [30] thought was diagnostic of juvenile verruca. In addition to all the foregoing observations, ordinary warts and plane warts in some cases have been associated with epidermodysplasia verruciformis.

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27. Hidaka, S.: Verruca Dyskeratoticae Congenitales, J. Orient. Med. **2**:281-288, 1924.

28. Freudenthal, W., and Spitzer, R.: Warzen und Kondylome, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 12, pt. 3, sect. 2, pp. 3-207.

29. Finnerud, C. W.: Epithelial Nevus, Arch. Dermat. & Syph. **37**:101-102 (Jan.) 1938.

30. Obermayer, M. E., in discussion on Finnerud.[29]

We have found the resemblance between the structure of verruca plana and that of epidermodysplasia verruciformis to be so frank as to oblige us to conclude that if the conditions are not identical, they are at least similar. Clinically, too, the resemblance is sharp, when it is considered that verruca plana may present a variety of shades, shapes and sizes, almost the counterpart of lesions of epidermodysplasia verruciformis. We feel, then, that the two conditions cannot be easily distinguished either on the strength of the histologic picture or on the appearance of the individual lesion. Certain features, however, are often associated with epidermodysplasia verruciformis which verruca plana does not ordinarily manifest: (1) the common onset in early life, with a history of parental consanguinity in some cases; (2) the frequent generalization; (3) the persistence of the eruption throughout life and its resistance to every form of treatment; (4) the failure thus far to perform inoculation experiments successfully, either on the same patient or on normal persons;[31] (5) certain, possibly quantitative, histologic differences, such as exaggeration of the vacuolar degenerative process in epidermodysplasia verruciformis, the predominance of pyknotic changes in the nuclei and the failure of investigators to observe inclusion bodies (Hoffmann and Kogoj, however, discovered acidophilic nuclei in swollen cells in their cases), and (6) the eventuation of epithelioma early in life in a significant number of instances of epidermodysplasia verruciformis, according to reports in the literature. Our experience does not include the last complication, and we suggest that it may perhaps be a feature allied to the form of disease described by Sézary and Lévy-Coblentz,[25] which may not belong to this group. As for the verruca plana, the possibility of malignant degeneration cannot be entertained at all.

In view of the foregoing analysis, we find it untenable to assume that we are concerned with one and the same disease, and we are therefore satisfied to regard epidermodysplasia verruciformis as a morbid entity separate from verruca plana. Undeniably, the significant single point of distinction is that connected with efforts at transference of the disease. If inoculation should ever be produced successfully with material taken from a lesion of epidermodysplasia verruciformis, thus resulting in demonstration of an infectious agent such as warts have, all these considerations will, of course, have been reduced to naught. In the absence of this indispensable phenomenon, proof is lacking that one is dealing here with two manifestations of a single condition ("verrucosis"). We therefore share the opinion of Wise and Satenstein and others that epidermodysplasia verruciformis is deserving of recognition as a distinct

31. Tornabuoni, G.: Epidermodisplasia verruciformis (Lewandowsky-Lutz), Gior. ital. di dermat. e sif. **70**:557-572, 1929. Hoffmann.[18] Kogoj.[20]

disease entity because of its ensemble of clinical traits. We are also convinced that much of the confusion in the literature is due to failure to distinguish disseminated verruca plana from true epidermodysplasia verruciformis.

A parallel instance of two different dermatologic conditions which present practically identical and distinctive histologic features is found in the occasional occurrence of a lesion of senile keratosis which microscopically simulates perfectly the picture of Darier's disease, as one of us (H. M.) [22] has recorded. It is not at all inconsistent, therefore, for two specific conditions, slightly or in no way related etiologically, to have an identical microscopic structure.

EPITHELIAL NEVI

Verrucous and papillomatous nevi were first systematically classified by Unna,[32] under the designation "hard nevi," in which group he included circumscribed warty protuberances with the microscopic appearance of purely epithelial thickening. Unna described the lesions as being clinically hard, flat, pink to gray or dark brown and of variable size, from that of a lentil to that of a palm, the surface being rough or finely granular. Histologically, he distinguished three types, determined by the site of epithelial proliferation, as the keratoid, the acanthoid and the mixed or combination form. Of Unna's three types, one or possibly two were verruca senilis, a lesion which may be a delayed epithelial nevus but which does not need to be discussed herein, since it presents its own distinctive histologic picture.[33] (Unna also identified the related "verruca dorsi manus et pedis," which he termed a systematized hard nevus appearing symmetrically in groups on the backs of the hands and feet. It was described as a small, flat, rounded or polygonal papule which appears on persons in middle or later life and does not further increase or completely disappear.) Microscopically, the prickle cell layer and especially the horny layer are thickened, and sometimes the granular layer also is increased; the cells otherwise are entirely normal (fig. 8 *a*). A patch or two of parakeratosis occasionally may be seen. Melanin is present both in the basal layer and in dendritic cells to account for the brownish color. The finely granular verrucous surface of the hard nevus may be scratched off with a curet, but the papule always recurs. Although such a lesion is commonly encountered, we believe that it is usually mistaken for verruca plana, flattened verruca vulgaris, senile keratosis or verruca senilis.

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32. Unna, P. G.: The Histopathology of the Diseases of the Skin, New York, The Macmillan Company, 1896.

33. Montgomery, H.: Verruca Senilis and Keratoma Senile, Minnesota Med. **18**:735-738 (Nov.) 1935.

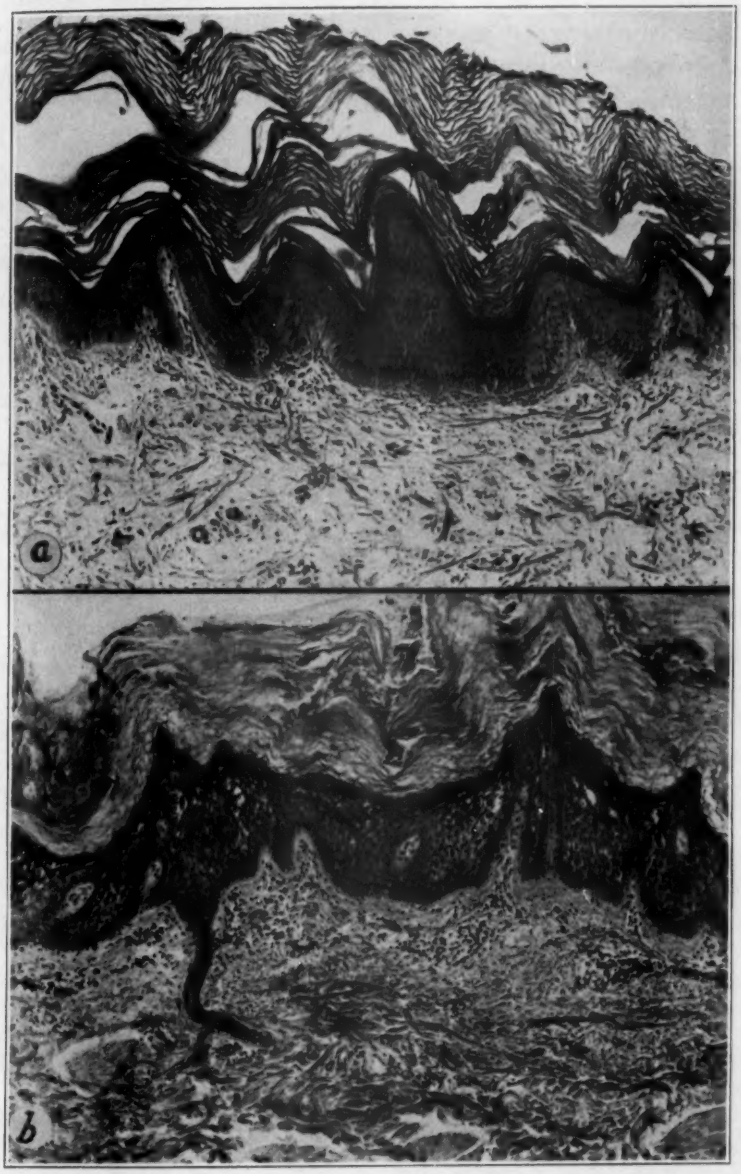

Fig. 8.—Epithelial nevi. *a*, section from a solitary hard nevus on the back of the hand of a woman aged 46; duration of the lesion unknown. Note the hyperkeratosis, increase in the granular layer and increased pigment in the basal layer; vacuolar degeneration is absent (hematoxylin and eosin, × 90). *b*, systematized epithelial nevus exhibiting hyperkeratosis, vacuolation and degenerative changes in the granular layer simulating those seen in verruca plana and epidermodysplasia verruciformis (hematoxylin and eosin, × 75).

Probably acrokeratosis verruciformis of Hopf [11] (the hyperkeratotic papule of which differs histologically from epidermodysplasia verruciformis in the absence of vacuolation) belongs in this extensive category of epidermal nevi or nevus-like structures, and conceivably so also does the discrete keratosis of the backs of the hands described by Michael [34] and the *naevus épidermohypertrophique* of Gougerot and Joannon.[35]

There is evidence that occasionally an isolated hard nevus may present the histologic appearance seen in epidermodysplasia verruciformis or verruca plana. Figure 109 in Gans's textbook illustrates this occurrence, with characteristic vacuolation of the epidermal cells. We have also seen one such epidermal nevus associated with a sebaceous nevus.

The structure and classification of epithelial nevi are reviewed by Gans.[36] They may be circumscribed or systematized (linear), the latter forms being unilateral by predilection. Among the circumscribed forms occur either small or giant structures, among which is included the keratoid hard nevus of Unna. The linear type of epithelial nevus is well represented in the case of Binzer,[37] in which histologically the vacuolar disintegration of the protoplasm was extreme. Binzer decided that normal keratohyalin could no longer be formed in the degenerating cells and that in its stead arose granular and threadlike bodies, behaving like keratohyalin, massed about the remaining nuclei or between the remnants of cells. But, although the life cycle of the epidermal cell obviously proceeded in an abnormal manner, the end product of the cycle, the stratum corneum, was apparently normal. The author conceived of a malformation inherently present in the germinal cells, becoming visible in the stratum spinosum.

Gassmann [38] minutely described this anomaly in a case of hyperkeratotic systematized nevus. Approximately half the width of the rete was taken up by the granular layer, the tinctorial reaction of which differed from that of normal keratohyalin. With the appearance of the first tiny granules the prickles were already gone, leaving only a poorly stained swollen membrane without intercellular spaces or prickles.

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34. Michael, J. C.: Discrete Keratoderma of the Dorsum of the Hands: A Probably Unrecognized Entity, Arch. Dermat. & Syph. **21**:215-227 (Feb.) 1930.

35. Gougerot and Joannon: Naevi épidermohypertrophiques des mains et des pieds, Rev. franç. de dermat. et de vénéréol. **2**:170-174, 1926.

36. Gans, O.: Histologie der Hautkrankheiten. Die Gewebsveränderungen in der kranken Haut unter Berücks ihrer Entstehung und ihres Ablaufs, Berlin, Julius Springer, 1927, vol. 2, pp. 228-231.

37. Binzer, E.: The Generalized Keratotic Nevus, Arch. Dermat. & Syph. **21**:413-418 (March) 1930.

38. Gassmann, A.: Histologische und klinische Untersuchungen über Ichthyosis und ichthyosisähnliche Krankheiten, Arch. f. Dermat. u. Syph. (supp.) **69**:3-218, 1904.

We have studied material obtained at biopsy in 2 such cases, the sections disclosing practically identical changes (fig. 8 *b*). In 1 of these cases the patient was an 11 year old boy over whose body papillomatous and verrucous lesions had first appeared, at the age of 6 months, as solid,

Fig. 9.—Systematized epithelial nevus affecting a boy 11 years of age. The histologic changes in the lesions were similar to those apparent in figure 8 *b*. Nevus cells were not present.

dark-hued plaques in some regions and as long, linear bands in others (fig. 9). Microscopically, the changes constituted an extreme example of the degenerative protoplasmic anomaly throughout the thickened granular layer (fig. 6 *b*). The edema appeared to be largely intracellular, but separation of cells by extracellular fluid also was apparent.

When the changes were pronounced, disorganization of the cellular relations occurred in the upper part of the prickle cell layer and in the stratum granulosum, so that portions of the stratum granulosum had the appearance of vesicular formation. Strands and granules of a keratohyalin-like material, which stained violet, occupied the region. A mild, spotted form of parakeratosis appeared in the stratum corneum.

COMMENT

Among epithelial nevi numerous morphologic types have been recognized, including many rare forms, and they have been classified on the basis of their structure, number and distribution. We have merely taken one histologic type of linear nevus and have indicated its relation to an apparently grossly distinct papular verrucous eruption, epidermodysplasia verruciformis.

The peculiar protoplasmic degeneration which all of our material displays makes for a common histologic bond which unites these different clinical forms in the group of epithelial nevi. Within this classification should be included epidermodysplasia verruciformis, some examples of hard nevus (Unna) and certain types of linear nevus.[39] A similar attempt at unification is attributed to Woronow,[40] who is stated to have perceived the histologic identity of epidermodysplasia verruciformis, linear dermatosis and naevus corneus. Further confirmation of this intimate relation is found in the case reported by Goeckerman,[41] in which both linear nevus and epidermodysplasia verruciformis occurred together.

The nature of the vacuolar degeneration of the epidermis is obscure, and histologic methods have not shed light on the changes. Earlier, in discussing epidermodysplasia verruciformis, we reviewed the various possibilities of pathogenesis of this dermatosis: eczematoid reaction, dyskeratosis, verrucose dermatosis and nevoid state. In view of our observations, we favor the classification of epidermodysplasia verruciformis as a form of epithelial nevus, and we are supported in this conclusion by the similar histologic appearances apparent in cases of linear nevus.

SUMMARY AND CONCLUSIONS

We have reviewed the similarities and differences which exist between epidermodysplasia verruciformis and verruca plana, both clinically and histologically, in an effort to determine whether the conditions are identical or distinct. It has become apparent to us that the two conditions

39. Mention should be made of another type of epithelial nevus with vacuolar changes, keratoderma palmare. Maschkilleisson and Kogoj recognized this histologic characteristic, and we too have observed it.

40. Woronow, cited by Maschkilleisson.[23]

41. Goeckerman, W. H., in discussion on Wise and Satenstein.[17]

may be adequately separated on clinical grounds in spite of decided microscopic resemblances, and we are therefore not in agreement with those authors who would classify epidermodysplasia verruciformis as a form of generalized or disseminated wart. The histologic relations between verruca plana and verruca vulgaris also have been studied, such study leading to the conclusion that the alterations, although they present many points in common, differ more than quantitatively. The "characteristic" parakeratosis of verruca vulgaris has not been observed in our cases of verruca plana.

Cellular changes in the epithelial nevi studied constitute a striking anomaly during the course of the keratinization cycle. With regard to epidermodysplasia verruciformis, the basis for these changes has been much disputed. Examination of certain epithelial nevi, of both the circumscribed and the linear form, indicates that pathologic changes may be present which are practically identical with those present in epidermodysplasia verruciformis. The vacuolar protoplasmic abnormality which each form manifests indicates the essential nevoid structure common to them.

We have also incidentally called attention to the so-called hard nevus of Unna, a flattened verrucous papule commonly appearing on the backs of the hands and wrists of persons in middle life or younger. Because these lesions are often erroneously identified as verruca plana, verruca vulgaris or senile or seborrheic keratosis, we believe our examination of their microscopic structure has been warranted.

ABSTRACT OF DISCUSSION

Dr. Marcus Rayner Caro, Chicago: We are indebted to Dr. Waisman and Dr. Montgomery for their exhaustive study, demonstrating the clinical and histologic relations between verruca plana, epidermodysplasia verruciformis and epithelial nevus. Their conclusion that epidermodysplasia verruciformis is a distinct entity rather than a form of extensive warts seems to be well established by their observations. The inclusion of this rare dermatosis among the varieties of epithelial nevus is justified by its clinical course and on histologic grounds.

The authors are to be commended on their study of verruca plana, a condition seen clinically every day and yet seldom investigated histologically. They are to be congratulated also for finding 4 cases of epidermodysplasia verruciformis, the diagnosis of which has heretofore been exceedingly rare but which will undoubtedly be made more often in the future.

It is possible that there may be patients with dermatoses under treatment by dermatologists in various parts of the country where the local facilities for histologic study are inadequate to arrive at a correct diagnosis. Rare diseases might become more commonly recognized or, at least, more readily diagnosed if there were available some central diagnostic registry to which biopsy specimens from unusual cases could be submitted for an opinion. Pioneer work in this direction was performed by a committee of the American Academy of Dermatology, which studied histologic sections accompanied by clinical histories and photographs sent

in by various members and which reported its diagnoses at a histologic seminar at the meeting in Chicago last year. It might be feasible to set up some such machinery for the use of all dermatologists.

It is true that a number of dermatopathologists do have sections submitted to them at times for diagnosis, but such opportunities for expert opinion must of necessity be relatively infrequent, for they are in the nature of a personal imposition. A central diagnostic registry composed of several dermatopathologists would invite a more general use of such help, and it would divide the burden of the work so as to make the project feasible. Such a committee would be in a position to winnow the entire field of dermatology, for although patients with rare dermatoses do not always find their way to the men best qualified to study them, the biopsy specimens from such patients with the accompanying histories and photographs could in this way be subjected to an early competent investigation. An interchange of ideas about individual cases between the various members of such a committee might also be of great benefit in eliminating minute and unsupportable differences of opinion.

American dermatology would take a great step forward if Dr. Montgomery, with the excellent facilities at his disposal, were to take the initiative in organizing a group to function as such a diagnostic registry.

DR. A. LOVEMAN, Louisville, Ky.: The reason I happen to be so interested in this paper is because I was fortunate enough to observe 2 cases within the past six months of a very rare, somewhat allied, dermatosis known as Hopf's acrokeratosis verruciformis. These cases were presented by Dr. Graham and me in a clinic at the Southern Medical Association meeting in Louisville, Ky., and a report was later published in the ARCHIVES (**43**:971 [June] 1941).

I should like to call attention to a few important criteria for differentiating this condition from epidermodysplasia verruciformis. Acrokeratosis verruciformis looks very much like epidermodysplasia verruciformis clinically. The lesions in both conditions are verrucous, resembling flat warts, and are usually found on the backs of the hands and on the dorsal surfaces of the feet. Acrokeratosis verruciformis, however, usually is accompanied by disseminated keratosis of the palms and soles. In epidermodysplasia verruciformis there are almost always large verruca vulgaris-like lesions. Furthermore, in epidermodysplasia verruciformis some of the lesions often become epitheliomatous.

Histologically acrokeratosis verruciformis does not show the basket weave vacuolization that epidermodysplasia verruciformis does, nor is there any parakeratosis of cellular degeneration. It would be nothing short of conceit to question the diagnosis in any of the aforementioned cases, and yet, since seeing some of the sections from the cases of Drs. Montgomery and Waisman, I am impressed with the close similarity of the changes to those seen in epidermodysplasia verruciformis. Perhaps these two conditions are variants of the same disease. Regardless of this, I agree with the authors that both conditions represent nevoid diseases of a verrucous nature. Hopf expressed a similar opinion in his early reports.

DR. F. A. ELLIS, Baltimore: Ordinarily verruca plana does not last as long as the lesions of acrokeratosis verruciformis (Hopf), described by Loveman. Although some flat warts of children may last for years, Memesheimer and Eisenlohr (*Dermat. Ztschr.* **62**:63, 1931) reported that 40 per cent healed spontaneously in six months.

In epidermodysplasia verruciformis there are usually more generalized and larger lesions than in verruca plana juvenilis. In the latter disease malignant

degeneration does not occur. The condition in the case reported by Dr. Sullivan and myself (ARCH. DERMAT. & SYPH. **40**:422 [Sept.] 1939) had been diagnosed verruca plana juvenilis before it was finally recognized by Dr. Fred Wise.

Histologically, there were certain features of value in the differentiation. In our case, in which the changes were more severe, the vacuolation had progressed further, and altered cells were much larger than those described by Drs. Waisman and Montgomery. The disintegration of the nuclei was much more severe. We found that some of the nuclei became pyknotic and others seemed to become fragmented, to break up and be disseminated within the cellular membrane instead of being pyknotic and pushed off to one side. The altered cells were at times deeper and extended practically to the basal layer. The changes are more superficial in verruca plana juvenilis. If the sections do not have areas that show these late changes, the differentiation may not be so easy.

DR. FRED D. WEIDMAN, Philadelphia: What a number of these various verrucoid conditions has been mentioned in the last half-hour! The presenters have named three and one of the discussers another; that is four. Moreover, I am sure that dermatologists have encountered numerous other kinds of verrucoid conditions that cannot be classified. I recall certain flat, wartlike lesions occurring in great numbers on the legs of an old woman who had not used soap, apparently, for a long time. It is my custom when I encounter such cases to refer to the Corpus Iconum Morborum Cutaneorum (Nékám, L.: Corpus Iconum Morborum Cutaneorum, Leipzig, Johann Ambrosius Barth, 1938) and see just how closely I can fit my immediate dermatologic problem with one of the conditions therein described. It generally turns out that there is not anything that accurately fits my peculiar condition. Accordingly, I dare say that a long list could be constructed, if every new example of a peculiar verrucoid condition were to be designated by a specific name and regarded as a separate entity.

Coming to the immediate problem, the histologic data have been submitted in considerable detail. Much of the discussion has centered on the matter of vacuolation. Now, "vacuolation" is only objective. The pathologist at large always attempts to go farther back than that; he tries to envisage what is behind the scene. What kind of pathologic process is concerned in inducing the vacuolation? Vacuolation can come about in various ways. It may be the result of intracellular edema; it may be the result of an artefact—undue shrinkage caused by the formaldehyde or whatnot—and, conceivably, it might be the result of intracellular metabolites of fluid nature, being not necessarily edematous and derived from surrounding tissues but elaborated actually within the cell.

If one approaches the problem from that angle, one is likely to get farther along in determining whether these verrucous entities are really such. After having decided that, one is on more solid ground for going ahead and trying to relate these verrucous conditions, and if, accordingly, one finds that in such a generalized systematized epithelial nevus the vacuolation is that of edema and that likewise in verruca plana there is a similar kind of pathologic process, there is then a more secure reason for claiming that the conditions are one and the same thing.

Now, applying the foregoing ideas to the presentation of Drs. Waisman and Montgomery, it appeared to me that in the case of the systematized nevus the process was the more truly edematous in nature. That is, the watery features were not confined so much to the interior of the cells but more interstitially, whereas in epidermodysplasia verruciformis it appeared to be more strictly intracellular. In any event, before one comes to a final conclusion, a considerable

number of lesions should be studied, and not lesions from simply one or two cases but from a series of cases. Then one can come to more substantial conclusions.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Dr. Waisman and I greatly appreciate all the discussions. Dr. Caro's suggestions regarding histologic diagnoses in unusual cases should, I believe, be taken up at the next meeting of the American Academy of Dermatology. In regard to intracellular edema in epidermodysplasia verruciformis, we believe that this is a benign dyskeratotic process and that the condition is essentially an epithelial nevus. Dr. Weidman correctly emphasizes that there is more intercellular than intracellular edema in the case illustrating a linear nevus, which may be of value in distinguishing the two conditions, and similarly pyknotic changes occur in the nuclei of epidermodysplasia, whereas there are no pyknotic changes in the nuclei of the vacuolated cells in verruca plana. Some authors have suggested that the condition may be a disturbance in the formation of the keratohyalin or that the keratohyalin may be of a different chemical nature in these various conditions. A larger series of cases of verruca plana should be studied histologically before definite conclusions are reached.

The case of epidermodysplasia verruciformis described by Sullivan and Ellis in the ARCHIVES histologically showed a definite squamous cell epithelioma in situ in many places with the phenomenon of malignant dyskeratosis. In some cases of Bowen's disease one may see intracellular edema of the cells without any malignant change or evidence of amitotic or mitotic cell division and yet adjacent cells will show all the latter features. In our cases of epidermodysplasia verruciformis and also in those of Wise and Satenstein there was no evidence of malignant dyskeratosis. Verruca plana is autoinoculable owing to a virus. Various authors have tried inoculation experiments in epidermodysplasia verruciformis without success. We were unable to do this in our cases, as they had been encountered some years ago and misdiagnosed clinically as cases of verruca vulgaris or of a peculiar type of epithelial nevus. Epidermodysplasia usually starts in infancy and generally involves the face and hands and presents a different clinical picture from verruca plana. Whereas the two simulate one another histologically, similar resemblances are observed, for example between the early stages of keratosis senilis and the hypertrophic stages of lichen planus. In regard to the hard nevus of Unna, the histologic sections reveal a wavy stratum corneum and no vacuolated cells, a distinctly different histologic picture from verruca plana. The histologic structure essentially duplicates that of acrokeratosis verruciformis of Hopf, which possibly may be simply an accentuation of a hard nevus. In recent specimens for biopsy, we have seen conditions clinically suggestive of the hard nevus which histologically showed early transition toward keratosis senilis on the one hand and toward lentigo on the other. This is not surprising if one realizes that multiple types of nevoid disturbances may occur in the same person.

PSEUDOXANTHOMA ELASTICUM

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AND
JUVENAL ESTEVES, M.D.
LISBON, PORTUGAL

Last year we reported [1] the first case of pseudoxanthoma elasticum which had come under our observation. The patient, a 27 year old woman, had cutaneous changes symmetrically located on the neck, in the axillas and on the elbows and knees which consisted of small faintly yellow papules, some of which were confluent. The skin in the affected areas was wrinkled and flaccid because of loss of elasticity. The eruption had appeared a short time after puberty. Histologically, the changes were the same as those Darier [2] termed elastoclasis, or elastorrhexis. The broken-up elastic fibers were thicker than normal and appeared edematous; they were scattered all through the cutis in clumps of various sizes. The most curious histologic feature was the manner in which fragmentation of the fibers had occurred. Clear, round spaces could be seen within the fibers in a rosary-like distribution; they were filled with a substance which distended the fiber and obviously lessened its resistance, for it was at the point of distention that the fibers had ruptured. This method of rupture was evidenced by the many fibers whose two ends showed concavities corresponding to the former clear space.

We suggested the following possible explanation for the pathogenesis of the changes in the elastic tissue: It seemed safe to assume that our patient had congenital syphilis; complement fixation and precipitation tests of the patient's blood gave positive results, and her father had died from dementia paralytica. It might be assumed that the patient had a syphilitic involvement of the anterior lobe of the hypophysis, which could have had effects on the cutaneous elastic tissue similar to those in Cushing's disease, or even in acromegaly.[3] Whether such effects are achieved directly by way of the hypophysial secretions or indirectly by an influence on the other endocrine glands has not been established. The indirect method seems probable in the case of our patient, whose low level of cholesterol in the blood seemed to indicate a decrease in the function of the adrenal cortex. According to experiments by Musger,[4] the adrenal cortex exercises a pronounced influence on elastic tissue.

From the Department of Cutaneous and Venereal Diseases of the Desterro Hospital.

1. de Sá Penella, L., and Esteves, J.: Actas dermo-sif. **31**:390, 1940.
2. Darier, J.: Ann. de dermat. et syph. **7**:1211, 1896.
3. Weber, F. P.: Brit. J. Dermat. **40**:1, 1928.
4. Musger, A.: Arch. f. Dermat. u. Syph. **177**:233, 1938.

A lesion of the pituitary gland could also have been the cause of the intermittent amenorrhea and sterility of our patient. The suggestion that a syphilitic hypophysial lesion may be responsible for such changes as were present in our case is not original with us, for such changes were known to Virchow.[5] Schmidt [6] reported that the incidence of hypophysial involvement in congenital syphilis was 47 per cent. Katzenstein [7] stated that only the anterior lobe is affected and that frequently no clinical symptoms are present, the changes being demonstrable only at autopsy.

Curiously enough, shortly after we had examined the patient whose case we have just briefly reviewed, another patient with pseudoxanthoma elasticum came under our observation.

REPORT OF A CASE

The patient was a widow, 43 years of age, who had always been in easy circumstances. Her parents were dead, and nothing of interest was elicited concerning them except that they were not consanguineous. One brother, who had died from pulmonary tuberculosis, had had cutaneous lesions identical with those of the patient; another brother was alive and well. A sister had died from peritoneal tuberculosis and meningitis. The patient's husband had died from pulmonary tuberculosis, and shortly before death his blood had shown a weakly positive Wassermann reaction and a strongly positive Kahn reaction. The patient had been married seventeen years and, like her brothers, was childless. She gave a history of conjunctivitis in childhood and of cervical adenitis, the scars of which were in evidence. The menarche occurred at the age of 13; she had never been pregnant. She stated that she had never had any previous cutaneous disease or syphilis, and no stigmas of congenital syphilis were present.

Physical examination revealed a normal-appearing, rather fat woman with ruddy cheeks, who looked about her age. She was 154 cm. tall and weighed 70 Kg. She showed no evidence of loss of weight. Her skin was dark and of the seborrheic type. Some pigmented nevi were present on the face and on the thorax.

On the sides of the neck and extending downward over portions of the shoulders and chest, on the abdomen and in the inguinal regions, axillas, bends of the arms and popliteal regions were cutaneous alterations which had been present unchanged since the patient was 16 years of age without giving rise to symptoms. The changes were most accentuated at the anterior borders of the axillas. The cutaneous alterations were distributed over a semicircular area around the umbilicus involving the hypogastric region and the flanks. At first glance the changes appeared to be exaggerations of the normal lines and folds of the skin; they were increased by flexion and decreased by hyperextension and abduction (fig. 1). The skin of the involved regions was a dirty brownish purple. Close examination showed the presence of many perifollicular round papules, 0.5 to 5 mm. in diameter, smooth surfaced and the color of old ivory. In many places they formed plaques of various sizes. The lesions were best seen at the periphery

5. Virchow, R.: Virchows Arch. f. path. Anat. **15**:299, 1858.
6. Schmidt, M. B.: Verhandl. d. deutsch. path. Gesellsch. **6**:207, 1904.
7. Katzenstein, R.: Virchows Arch. f. path. Anat. **289**:222, 1933

of the involved area, where they were not confluent; some of them were erythematous. The affected areas when viewed by oblique light had the uneven and granulated appearance of *"peau de chagrin."* In the region of the abnormal folds the skin was flabby and easily stretched. The involved areas were not tender and were characterized by a scarcity of hair, particularly in the axillas.

On the oral mucosa, especially in the gingivolabial groove and on the inner surface of the lower lip, there were lesions identical with those on the skin. They consisted of groups of round, slightly elevated papules, which were regular in outline and the color of egg yolk; on their surfaces fine telangiectases were seen.

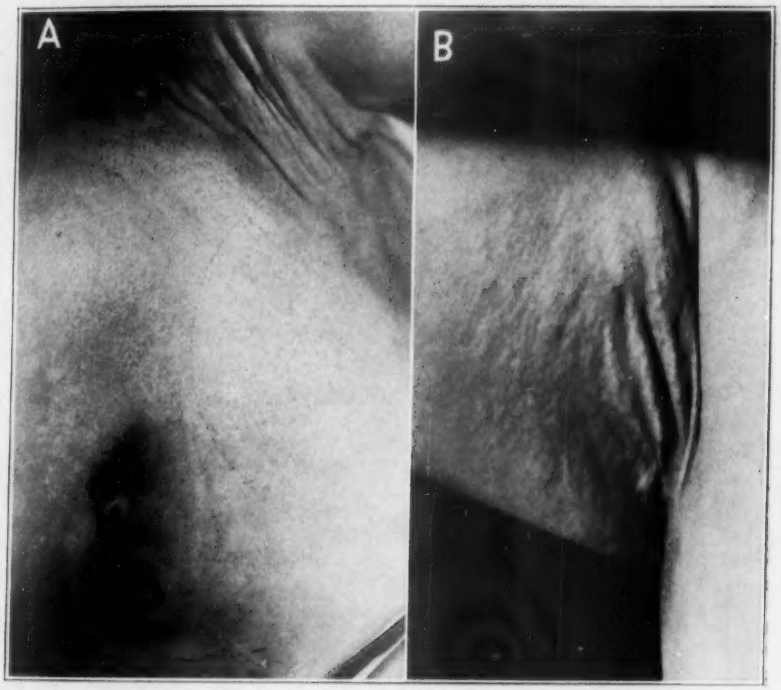

Fig. 1.—Cutaneous changes resembling exaggeration of the normal lines and folds of the skin. *A*, neck and axilla. *B*, right axilla. The skin has the uneven, granulated appearance of *"peau de chagrin."* Note the scarcity of axillary hair.

The changes in the elasticity of the skin suggested the possibility that the elastic tissue in other regions might also be involved, as in the syndrome which Godin [8] described in 1928 and characterized as an alteration in all the elastic tissues of the body. The elements of this syndrome are: flaccidity of the auricles and of the normal-appearing skin, which, however, is fragile and has a tendency to split; relaxation of the abdominal wall and enlargement of the abdominal rings, with

8. Godin: Le tissu élastique, son importance clinique, Paris, A. Maloine et fils, 1929.

production of hernias, abnormal motility of the joints with a tendency toward luxation, subluxation, kyphosis and scoliosis; muscular atony; vascular dilatation, evidenced by varices and hemorrhoids; gastrectasis with gastrointeroptosis; easy fatigability; a low level of cholesterol in the blood, and symptoms referable to the pituitary gland.

Except for the cutaneous changes, detailed examination of our patient revealed no other symptoms of Godin's syndrome except flaccidity of the auricles and of the abdominal wall. Roentgen examination of the sella turcica showed no alterations in its appearance or dimensions.

Except for the lesions previously described and a few decayed teeth, examination of the mouth showed nothing abnormal. The roentgenograms[9] of the gastrointestinal tract and the liver were normal. Roentgen examination of the lungs showed a calcified gland in the left hilus and a shadow at the level of the second rib on the left, the result of apical pleurisy, but no sign of a paren-

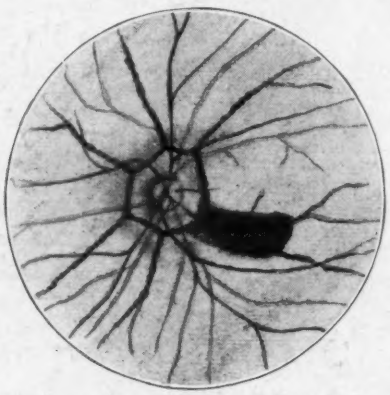

Fig. 2.—Drawing of the retina, showing the typical angioid streaks of the vascular type.

chymatous lesion. The heart and aorta were of normal dimensions and without roentgenologically demonstrable abnormality. Examination of the genitourinary tract showed nothing unusual, and the patient gave a history of a regular, copious menstrual flow. Neurologic examination gave normal results.

Ophthalmologic examination, the results of which were confirmed by Dr. Henrique Montinho, disclosed typical angioid streaks of the retina of the vascular type (fig. 2). Vision in the left eye was 5/20, and with the right eye the patient could distinguish fingers at a distance of only 2 meters. Myopia and astigmatism were demonstrated.

The reaction to the Krankl-Hochwart test, performed by injecting intramuscularly 2 cc. of a 5 per cent solution of an anterior pituitary extract,[10] was negative; that is, there was no rise in temperature indicating dysfunction of the pituitary gland. The reaction to the Loewi test, carried out by instilling 3 drops and five minutes later 3 more drops of a 1:1,000 solution of epinephrine hydrochloride into the conjunctival sac, was likewise negative.

9. All roentgenologic examinations were carried out by Dr. Ayres de Sousa.

10. "Byla" was the preparation used.

The basal metabolic rate was +7 per cent.[11] The reactions to the Wassermann and Kahn tests were negative. The hemoglobin content, color index and erythrocyte, leukocyte and differential counts were all normal. Chemical examination of the blood showed 200 mg. of cholesterol, 11.2 mg. of calcium and 80 mg. of dextrose per hundred cubic centimeters. The results of urinalyses were normal.

Histologic examination[12] of a specimen from the involved area showed that the epidermis was irregularly thinned and in some areas consisted of only three

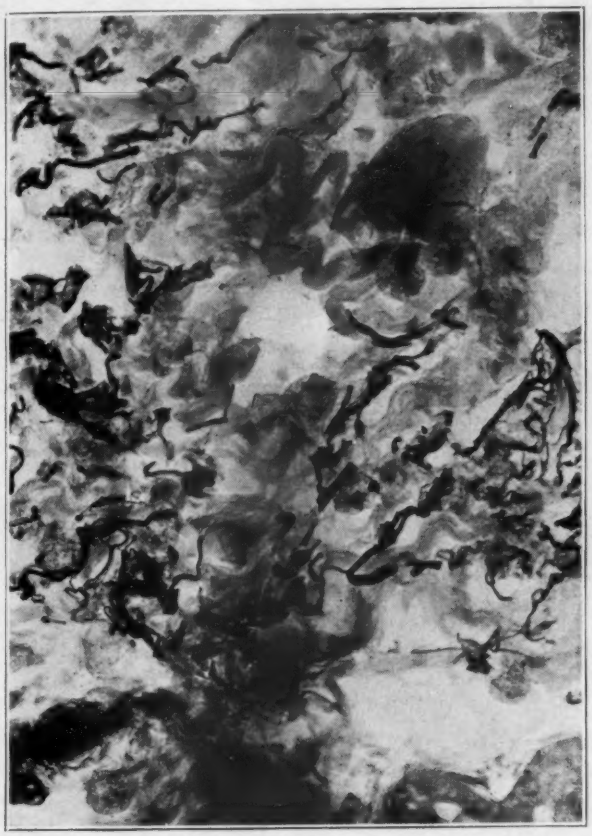

Fig. 3.—Section of the cutis, showing fragmentation and twisting of the elastic fibers (× 210).

layers of cells. The stratum corneum was rather delicate, and the stratum granulosum was everywhere reduced to a single cellular layer. The papillary layer of the cutis showed normal papillae and fine interlaced collagen fibers, with no signs

11. Dr. Joao Alvin and Prof. Roberto Chavez carried out all the laboratory examinations.

12. The histologic examination was carried out in collaboration with Dr. Xavier Morato.

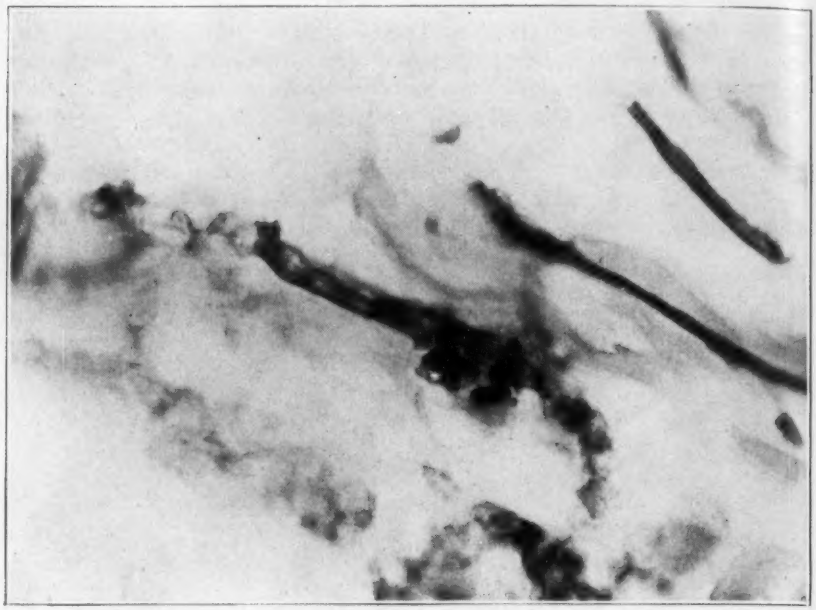

Fig. 4.—Section of the cutis, showing the nonhomogeneous absence of staining in the elastic fibers (× 1,150).

Fig. 5.—Section of the cutis, showing rosary-like appearance of the elastic fibers (× 1,150).

of inflammation or edema. The sweat and sebaceous glands appeared normal; the capillaries were surrounded by a fringe of fibroblasts. No giant cells were seen. Deep in the cutis there were zones in which the collagen fibers stained less deeply with eosin and, on the contrary, more deeply with hematoxylin. In those irregular and relatively ill demarcated zones the individual bundles of collagen tissue were not sharply defined and seemed to have undergone hyaline degeneration. There was also an increase in fibroblasts.

The elastic tissue was stained by Weigert's resorcinol-fuchsin stain. In the stratum papillare the relatively thick filaments of elastin had a reticular arrangement. In the deeper layers the bulky elastic fibers, which were lighter colored than normal, were fragmented and twisted, so that they assumed no real reticular arrangement (fig. 3).[13] In the zones of the cutis previously described, which

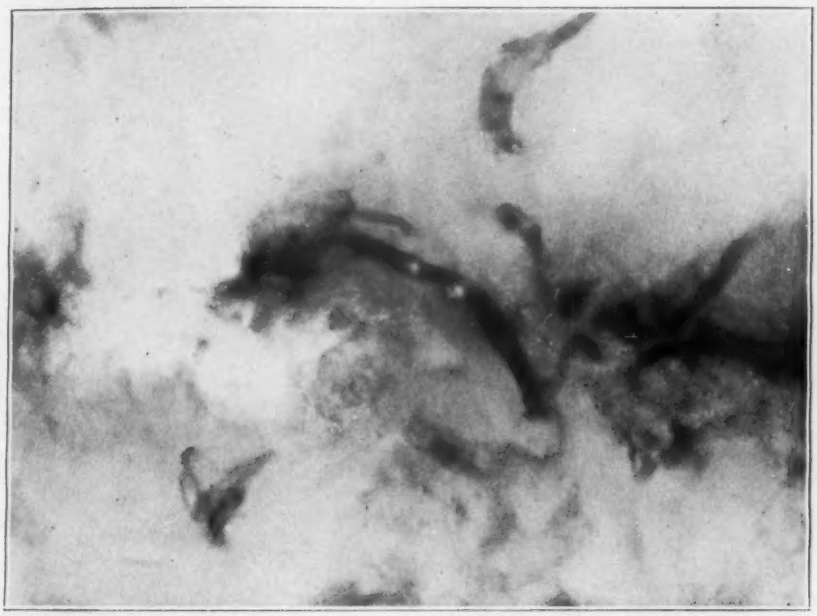

Fig. 6.—Section of the cutis, showing the herniation through the sheath of elastic tissue of the substance filling the clear, beadlike spaces (× 1,000).

stained more deeply with hematoxylin, the alterations in the elastic fibers reached their highest point. In these regions the fibers were completely broken up into small fragments and showed a pronounced loss of staining ability. In those fragments large enough to be examined, it could be seen that the absence of staining was not homogeneous; it was the series of noncontinuous spots corresponding to the distended central portions of the thickened fiber which did not take the stain and which gave to the fiber the appearance of a rosary (figs. 4 and 5). These rosary-like alterations in the fibers, which were identical in every respect with those observed in our first case of pseudoxanthoma elasticum, were especially apparent in regions where there was much degenerated, poorly staining

13. All of the photomicrographs were prepared at the Institute of Histology of the Faculty of Medicine, University of Lisbon.

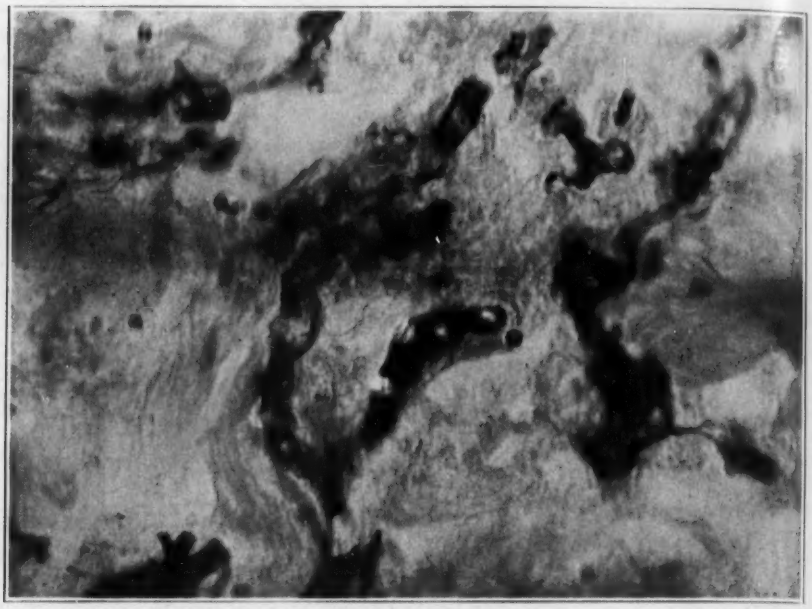

Fig. 7.—Section of the cutis (× 1,000), illustrating the succession of steps resulting in the ultimate rupture of the elastic fiber (for detailed explanation see text).

Fig. 8.—Section of the cutis typical of the areas in which the elastic fibers were somewhat fragmented but not completely broken up; they still stained uniformly, and there was no evidence of the vacuolar process (× 1,150).

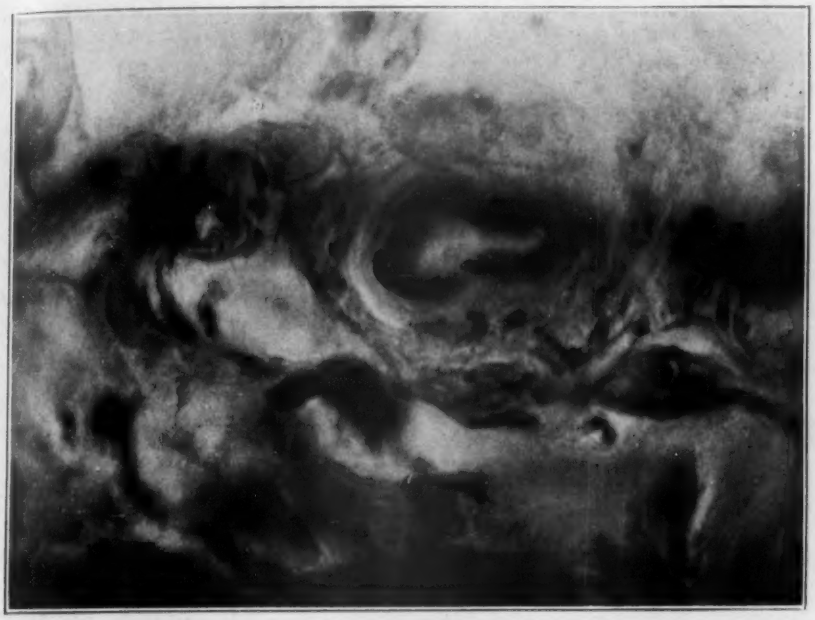

Fig. 9.—Section of the cutis, showing thickening and fragmentation of the elastic tissue fibers of a small artery (× 1,150).

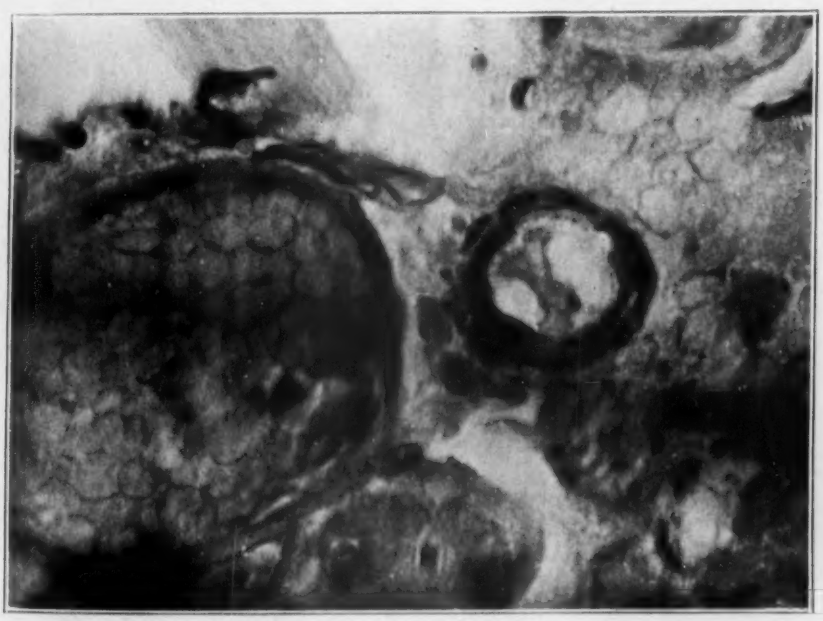

Fig. 10.—Section of the cutis, showing pronounced alterations in the elastic fibers of the adventitia and media of an arteriole and the unaltered walls of the nearby vein (× 1,150).

elastin. As was pointed out previously in commenting on our first case, this beadlike distention of the fiber is the first step in its reduction to shapeless fragments, for it is at these points of greatest distention that resistance is lessened and the fiber ruptures.

Sometimes (fig. 6) one could see the manner in which the substance filling the clear beadlike spaces herniated through the sheath of elastic tissue. In figure 7 one may follow the successive steps leading to rupture of the fiber. At the right of the figure is a clear, distended area still included within the thin sheath of the elastic fiber. Nearby are two vacuoles in which the included substance is bulging toward the outside. Finally one sees the terminal stage, with rupture of the fiber and evacuation of the lighter-staining substance which had been included in the vacuole. Noticeable is the hollow, semilunar shape of the two ends of the fragmented fiber. Such concave ends of fragmented fibers were observed in many of the sections. In some sections (fig. 8), in which the fibers were somewhat fragmented but had not been completely broken up and still took the stain, the vacuolar process was not observed; in such areas the fibers stained uniformly.

The elastic tissue fibers of the small arteries also showed thickening and fragmentation (fig. 9). The adventitia and media of the arteriole in figure 10 showed pronounced alterations in their elastic fibers, while the walls of the nearby vein, which of course lack elastic fibers, showed no changes.

Histochemical analyses for lipoids, amyloid and calcium gave negative results. The absence of calcium is at variance with the results of Finnerud and Nomland,[14] who demonstrated the presence of an abnormal amount of calcium in the involved areas in 2 cases of pseudoxanthoma elasticum. Colloid degeneration of the elastic tissue could not be demonstrated.

COMMENT

The present case differs from our first case of pseudoxanthoma elasticum in that associated angioid streaks were present. Such streaks were described some forty years ago, but it was not until 1924 that Grönblad [15] pointed out the association of the choroid lesions with the cutaneous changes first described by Darier. The ocular lesions, like the cutaneous changes, result from alterations in the elastic tissue; and, as was emphasized by Benedict and Montgomery,[16] both pseudoxanthoma elasticum and angioid streaks may occur independently. Two such cases of dissociated angioid streaks were recently reported by Lopez de Andrade.[17] The alterations in elastic tissue in cases of pseudoxanthoma elasticum are not limited to the skin and the fundus. Vascular and cardiac localizations have been described by Balzer,[18] Herxheimer

14. Finnerud, C. W., and Nomland, R.: Pseudoxanthoma Elasticum: Proof of Calcification of Elastic Tissue; Occurrence With and Without Angioid Streaks of the Retina, Arch. Dermat. & Syph. **35**:653 (April) 1937.

15. Grönblad, E.: Acta ophth. **7**:329, 1929.

16. Benedict, W. L., and Montgomery, H.: Am. J. Ophth. **18**:205, 1935.

17. Lopez de Andrade: Bol. Soc. portug. de oftal. **2**:40, 1940.

18. Balzer, F.: Arch. de physiol. **4**:65, 1884.

and Hell,[19] Urbach and Wolfram [20] and Urbach and Nékám.[21] In both of our cases alterations in the elastic coat of the cutaneous blood vessels were observed but no changes in the aorta could be demonstrated. One may conclude that pseudoxanthoma elasticum, a syndrome due to alterations of the elastic tissue, is characterized by manifold localizations and manifestations throughout the body.

The histologic alterations in the elastic tissue were identical in our 2 cases. The continuity of the fibers was interrupted at frequent intervals by poorly staining, beadlike distentions. It was at these points of distention, where degeneration had already occurred, as was evidenced by the failure of the fibers to take the stain, that rupture of the fiber with evacuation of the contents of the vacuole took place. The nature of the substance included in the clear vacuoles or beads has never been established. Bloch [22] and Pautrier and Woringer [23] expressed the belief that an abnormal substance circulating in the blood and having a special affinity for the elastic tissue accumulated in them, swelled and utimately destroyed them. The substance seems not to be a lipoid, an amyloid or calcium. Since the histochemical examinations which we carried out shed no light on the nature of this material, we have come to the conclusion that instead of an accumulation of an unknown substance in the fibers there is a kind of intermittent, hydropic degeneration which terminates in the breaking up of the fibers into small fragments. The rosary-like, or beadlike, form taken by the altered fibers has been described by several authors, and Darier [2] even mentioned that vacuoles are sometimes formed. However, all previous authors have reported that fragmentation of the fibers took place at the point of strangulation and not, as in our cases, exactly at the level of the clear, beadlike swellings.

Darier stated that either syphilis or tuberculosis, acting on the endocrine system, might be considered to be the cause of the alterations belonging to the syndrome which he described. The existence of congenital syphilis was satisfactorily demonstrated in our first case of pseudoxanthoma elasticum. There was no evidence of syphilis in the present case, but there was a strong likelihood that the patient had had tuberculosis, since her husband and her brother had died from pulmonary tuberculosis and she had had cervical adenitis and at the time of writing had signs of apical pleurisy on the left side. In the present case there was no roentgenologically demonstrable hypophysial lesion and the reaction to the Krankl-Hochwart test was negative; but sterility was present,

19. Herxheimer, K., and Hell, F.: Arch. f. Dermat. u. Syph. **111**:761, 1912.

20. Urbach, E., and Wolfram, S.: Arch. f. Dermat. u. Syph. **176**:167, 1937.

21. Urbach, E., and Nékám, L., Jr.: Dermat. Wchnschr. **103**:1416, 1936.

22. Bloch, B.: Dermat. Wchnschr. **63**:713, 1916.

23. Pautrier, L. M., and Woringer, F.: Bull. Soc. franç. de dermat. et syph. **43**:864, 1936.

and this may have been an indication of insufficient production of hormones by the hypophysis, the anterior lobe of which has been characterized by Aschheim and Zondek as the main spring of sexuality.

Since, as Bodin [24] stated, the hypophysis influences elastic tissue, an insufficiency in hypophysial function might be responsible for the alterations in the elastic tissue in this case. Unlike our first case, in this case there was no hypocholesteremia or other indication that the hypophysis had disturbed the function of the adrenal cortex. Consequently, any influence of the hypophysis on the elastic tissue must have been exercised directly through its hormones and not, as the experiments of Musger [4] suggested, by way of the adrenals.

It is interesting that our 2 cases of pseudoxanthoma elasticum support Darier's theory of the pathogenesis of the disease in that there was evidence of the presence of syphilis in the first and of tuberculosis in the second.

SUMMARY

A case of pseudoxanthoma elasticum with associated angioid streaks of the retina is reported. In addition to the classic cutaneous lesions, alterations in the tunica elastica of the arterioles and deformation and fragmentation of the elastic fibers were observed. The changes in the elastic fibers were due to intermittent hydropic degeneration, which gave them a rosary-like appearance; it was through these distended, beadlike portions that rupture of the fiber, with evacuation of its contents, occurred.

Tuberculosis should be considered a possible causative factor in this case.

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24. Bodin, E.: Ann. de dermat. et syph. **1**:1073, 1900.

NUTRITIONAL DERMATOSES IN THE RAT

V. SIGNS AND SYMPTOMS RESULTING FROM A DIET CONTAINING UNHEATED DRIED EGG WHITE AS THE SOURCE OF PROTEIN

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AND
JANE NICHOLLS, M.Sc.
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The use of egg white as a foodstuff for experimental animals had its origin in the nutritional investigations of the early part of this century, when biochemical research was concerned chiefly with the problem of nitrogen metabolism. The deleterious effects of unheated or uncoagulated egg white were gradually realized after numerous investigators had reported poor growth, loss of weight, hypochlorhydria, vomiting, diarrhea, "poor utilization," dermatitis, conjunctivitis, abscesses, diminished hemoglobin, spasticity, failure of lactation, nephritis and death in experimental animals from its use as the entire ration or as the source of protein in various diets.

In the course of experiments on phosphorus retention, Steinitz [1] in 1898 observed that the ingestion of raw egg white by dogs caused vomiting and diarrhea. Falta and Noeggerath [2] in 1905 were unable to maintain adult rats on diets containing dried egg white as the sole source of protein; conjunctivitis and subcutaneous abscesses developed before death. Knapp in 1908 observed diarrhea and conjunctivitis when egg white was fed to adult rats.[3] In 1912 Maignon [4] reported that rats

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From the Department of Dermatology, Johns Hopkins University School of Medicine, and the Department of Biochemistry, Johns Hopkins University School of Hygiene and Public Health.

1. Steinitz, F.: Ueber das Verhalten phosphorhaltiger Eiweisskörper im Stoffwechsel, Arch. f. d. ges. Physiol. **72**:75, 1898.

2. Falta, W., and Noeggerath, C. T.: Fütterungsversuche mit künstlicher Nahrung, Beitr. z. chem. Physiol. u. Path. **7**:313, 1905.

3. Knapp, P.: Experimenteller Beitrag zur Ernährung von Ratten mit künstlicher Nahrung und zum Zusammenhang von Ernährungsstörungen mit Erkrankungen der Conjunctiva, Ztschr. f. exper. Path. u. Therap. **5**:147, 1908.

4. Maignon, F.: Rôle des graisses dans l'utilization de l'albumine alimentaire, Compt. rend. Soc. de biol. **72**:1054, 1912.

fed egg white exclusively lost 40 per cent of their body weight and died. Frank and Schittenhelm [5] in 1912 fed diets containing 25 per cent fresh or heated egg white to rats aged 6 to 8 weeks. The animals died within a month. Studying the influence of proteins on nitrogen excretion in the urine, Mendel and Lewis [6] in 1913 remarked the indigestibility of raw ovalbumin and poor utilization of egg white when it was fed to dogs. Hartwell [7] in 1921 showed that when lactating rats ate raw egg white they were unable to nourish their young. Bond [8] in 1922 fed raw egg white rations to rats and observed diarrhea and little or no growth.

Prompted by the earlier work of Steinitz and of Mendel and Lewis, Bateman [9] made extensive studies of the digestibility and utilization of egg proteins in various species. He showed that the ingestion of native egg white by dogs was followed by diarrhea and that only 50 to 70 per cent of it was utilized, the remainder being excreted in the feces. When the egg white was dried at high temperatures or thoroughly cooked, the protein was well utilized and did not cause diarrhea. Precipitation or coagulation with alcohol, ether or chloroform or incubation with dilute acids or alkalis rendered the egg white digestible. When Bateman fed healthy adult rats diets containing amounts up to 60 per cent of raw egg white, diarrhea occurred. When cooked egg white was fed, all the rats gained weight and none had diarrhea. He fractionated samples of egg white and found that the ovalbumin and conalbumin were the harmful fractions, whereas the ovomucoid and globulin caused no digestive disturbance.

While conducting experiments on calcium and phosphorus retention in rats, Boas [10] used Chinese dried egg white as a source of protein in the diet. She found that when 3 week old rats were fed an apparently normal diet containing 20 per cent of the dried commercial egg white, there resulted a disease the most striking symptoms of which were dermatitis, abnormal posture and gait and spasticity of the limbs. In

5. Frank, F., and Schittenhelm, A.: Ueber die Brauchbarkeit tief abgebauter Eiweisspräparate für die Ernährung, Therap. Monatsh. **26**:112, 1912.

6. Mendel, L. B., and Lewis, R. C.: Rate of Elimination of Nitrogen as Influenced by Dietary Factors, J. Biol. Chem. **16**:55, 1913-1914.

7. Hartwell, G. A.: Excess Protein and Mammary Secretion, Biochem. J. **15**:564, 1921.

8. Bond, M.: A Modification of Basal Diet for Rat Feeding Experiments, Biochem. J. **16**:479, 1922.

9. Bateman, W. G.: The Digestibility and Utilization of Egg Proteins, J. Biol. Chem. **26**:263, 1916.

10. Boas, M. A.: An Observation on the Value of Egg White as the Sole Source of Nitrogen for Young Growing Rats, Biochem. J. **18**:422, 1924.

order to determine the mechanism of the production of the disease, Boas [11] made studies with 600 rats and found that coagulation of the egg white rendered it innocuous and that the inclusion of certain foodstuffs, such as raw potato, potato starch, arrow root, dried yeast, egg yolk and milk, in a diet containing uncooked egg white counteracted the ill effects. Thus she postulated the presence of a protective "factor X" in the foods which neutralized the "toxic" property of the egg white.

Apparently unaware of Boas' observations, Friedberger [12] fed diets composed entirely of raw eggs to young rats and produced a disease the description of which corresponded closely to that described by Boas. When the eggs were cooked the disease was not produced. In 1927 Scheunert and Wagner [13] observed the same disease in rats that were fed diets composed exclusively of egg white. Stenqvist [14] described similar signs and symptoms in young rats fed whole raw eggs.

In the course of experiments on rickets in rats, György [15] in 1927 employed a diet containing uncooked egg white as the sole source of protein. He encountered a disease characterized by dermatitis, loss of weight and muscular hypertony, especially of the hind extremities. In collaboration with Gans he studied the microscopic appearance of the involved skin and found hyperkeratosis, parakeratosis and abundant amounts of sudanophilic, as well as anisotropic, fat in the stratum corneum and in the upper portion of the epidermis. In the period from 1927 to 1935 he produced the disease in 5,000 rats and made extensive studies concerning the question of therapy and the properties of the healing factor.[16]

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11. Boas, M. A.: The Effect of Desiccation upon the Nutritive Properties of Egg White, Biochem. J. **21**:712, 1927.

12. Friedberger, E.: Ueber den Anschlagswert und über Nährschäden bei einseitiger Verfütterung von Hühnerei, Deutsche med. Wchnschr. **52**:1760 (Oct. 15) 1926.

13. Scheunert, A., and Wagner, E.: Ueber den Einfluss des Kochens auf den Nährwert des Hühnereies, Deutsche med. Wchnschr. **53**:1258 (July 22) 1927.

14. Stenqvist, F.: Roh und gekochte Hühnereier als einziges Nährungsmittel für wachsende Ratten, Deutsche med. Wchnschr. **54**:1920 (Nov. 16) 1928.

15. György, P.: Stoffwechsel und Immunobiologie der Haut, in von Pfaundler, M., and Schlossmann, A.: Handbuch der Kinderheilkunde, Berlin, F. C. W. Vogel, 1935, vol. 10, p. 45.

16. (*a*) György, P.: The Curative Factor (Vitamin H) for Egg White Injury, with Particular Reference to Its Presence in Different Foodstuffs and in Yeast, J. Biol. Chem. **131**:733 (Dec.) 1939. (*b*) György, P.; Kuhn, R., and Lederer, E.: Attempts to Isolate the Factor (Vitamin H) Curative of Egg White Injury, ibid. **131**:745 (Dec.) 1939. (*c*) Birch, T. W., and György, P.: Physicochemical Properties of the Factor (Vitamin H) Curative of Egg White Injury, ibid. **131**:761 (Dec.) 1939.

In 1931 Parsons fed young rats diets containing as much as 66 per cent egg white.[17] The majority of the animals died within a few days unless a small amount of liver was included in the ration of the mother or fed to the young rats immediately after weaning. Rats thus protected from the initial overwhelming injury survived to show the cutaneous signs and "spasticity" previously described by other investigators. Subsequently Parsons and her collaborators Lease and Kelly made studies of the distribution of the protective factor in foods and attempted to determine its chemical nature and the nature of the injurious fraction of egg white.[18] With Almon, Parsons performed experiments designed to test the hypothesis of an allergic cause of the lesion and observed no correlation between hypersensitivity to egg white and the signs of injury.[19]

Findlay and Stern[20] made a study to determine the similarity between this disease in rats and pink disease in man. They described extensive neurologic changes in rats with egg white injury.

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17. Parsons, H. T.: The Physiological Effects of Diets Rich in Egg White, J. Biol. Chem. **90**:351 (Jan.) 1931.

18. (*a*) Parsons, H. T., and Kelly, E.: The Effect on Dermatitis of Heating Egg White, Am. J. Physiol. **104**:150 (April) 1933. (*b*) Parsons, H. T.; Lease, J. G., and Kelly, E.: Cure of Dermatitis Due to Egg White by Various Foodstuffs, J. Biol. Chem. **100**:lxxvii (May) 1933. (*c*) Parsons, H. T., and Kelly, E.: The Character of the Dermatitis-Producing Factor in Dietary Egg White as Shown by Certain Chemical Treatments, ibid. **100**:645 (May) 1933. (*d*) Lease, J. G., and Parsons, H. T.: The Extraction of a Factor Curative of Dermatitis in Rats Due to Egg White, ibid. **105**:1 (May) 1934. (*e*) Parsons, H. T., and Lease, J. G.: Variations in the Potency of Certain Foodstuffs in the Cure of Dermatitis Induced in Rats by Dietary Egg White, J. Nutrition **8**:57 (July) 1934. (*f*) Lease, J. G.; Kelly, E., and Parsons, H. T.: Effects on Three Types of Animals of Injection of the New Factor Curative of Pellagra-Like Symptoms Due to Egg White, J. Biol. Chem. **114**:lxi (May) 1936. (*g*) Parsons, H. T.: Comparison of Antitryptic Activity of Egg White with Its Capacity to Produce Characteristic Nutritional Disorder, ibid. **116**:685 (Dec.) 1936. (*h*) Lease, J. G.: Some Observations on Nature and Partial Isolation of a Substance Curative of Pellagra-Like Condition Due to Dietary Egg-White, Ztschr. f. Vitaminforsch. **5**:110 (April) 1936. (*i*) Parsons, H. T.; Lease, J. G., and Kelly, E.: The Effect of the Concentration of Dietary Egg White on the Need for a Protective Factor Given Orally or Parenterally, J. Nutrition (supp.) **13**:14 (June) 1937. (*j*) Parsons, H. T., and Kelly, E.: The Interrelation Between Dietary Egg White and the Requirement for Protective Factor in the Cure of the Nutritive Disorder Due to Egg White, Biochem. J. **31**:424 (March) 1937. (*k*) Parsons, H. T.; Gardner, J., and Walliker, C. T.: Possible Significance of Fecal Concentrations of the Factor Protective Against Egg White Injury, J. Nutrition (supp.) **19**:19 (April) 1940.

19. Almon, L., and Parsons, H. T.: Lack of Correlation Between Hypersensitivity to Egg White and Symptoms of Injury, J. Allergy **8**:547 (Sept.) 1937.

20. Findlay, C. M., and Stern, R. O.: Syndrome in Rat Resembling Pink Disease in Man, Arch. Dis. Childhood **4**:1 (Feb.) 1929.

Salmon and Goodman [21] reported that when young rats were suddenly weaned to diets containing as little as 18 per cent raw, dried egg white and allowed to eat unrestricted amounts of the diet, there developed a hemorrhagic nephritis and death in eight to fifteen days. When the weaning was gradual and the total intake was restricted during the first few weeks, the initial injury was avoided and the rats later showed the characteristic cutaneous signs. The severity of the cutaneous lesion was decreased and the character altered somewhat by the presence of small amounts of linseed oil, 18 per cent butterfat or hydrogenated cotton seed oil in the diet. Hypochlorhydria and diminution of hemoglobin occurred late in the disease.

Egg white injury has been reported in several species. Tully and Franke,[22] Lease and Parsons,[23] Lease,[24] Eakin, McKinley and Williams [25] and others produced severe dermatitis in chicks. Lease, Parsons and Kelly [26] described dermatitis in rabbits, monkeys and guinea pigs, and it is reported that Schultz [27] produced dermatitis in dogs.

Studies of the chemical and physical properties of the protective factor were made independently by Parsons and her associates [28] and by György and his collaborators.[16] Lease [18h] found that in its native state the material was insoluble in water, alcohol or other organic solvents but that hydrolysis with acid or digestion with proteolytic enzymes released a water-soluble material which was active when administered either orally or parenterally. György and his associates reported similar observations regarding the solubility of the active factor, which they designated "vitamin H." [16a, b] Autolysis of yeast yielded the factor as a water-soluble substance. It was released from liver by proteolytic digestion, treatment with hydrochloric acid or autoclaving at high temperatures.[16a] Electrodialysis of a concentrate indicated that the

21. Salmon, W. D., and Goodman, J. G.: Studies of the Raw Egg White Syndrome in Rats, J. Nutrition **8**:1 (July) 1934.

22. Tully, W. C., and Franke, K. W.: A Nutritional Disease Demonstrating a Feed Deficiency in Dried Eggs, Poultry Sc. **8**:343, 1934.

23. Lease, J. G., and Parsons, H. T.: The Relationship of Dermatitis in Chicks to Lack of Vitamin B_2 and to Dietary Egg White, Biochem. J. **28**:2109, 1934.

24. Lease, J. G.: Prevention by Egg Yolk of the Dermatitis in Chicks Due to Egg White, Poultry Sc. **16**:374 (Nov.) 1937.

25. Eakin, R. E.; McKinley, W. A., and Williams, R. J.: Egg White Injury in Chicks and Its Relationship to a Deficiency of Vitamin H (Biotin), Science **92**:224 (Sept. 6) 1940.

26. Lease, J. G.; Parsons, H. T., and Kelly, E.: Comparison in Five Types of Animals of the Effects of Dietary Egg White and of a Specific Factor Given Orally or Parenterally, Biochem. J. **31**:433 (March) 1937.

27. Schultz, F., cited by György,[16a] p. 734.

28. Footnote 18 *b, c, d, e, f, h* and *i*.

active factor was an ampholyte with an isoelectric point between p_H 3.0 and 3.5.[16c] Elementary analysis of a potent concentrate established it to be free from sulfur and phosphorus.[16c] By treatment with sulfuric acid and various adsorbents, György, Kuhn and Lederer [16b] prepared a potent concentrate, one rat day dose of which was contained in 30 to 40 micrograms of dry material. György, Melville, Burk and du Vigneaud [29] remarked a close parallelism between the chemical and physical properties and the natural distribution of the protective factor (vitamin H) and of biotin, a well known yeast nutrilite or growth factor of the bios group.[30] Extraordinarily small amounts of biotin are present in the richest sources, and extremely small doses suffice for stimulation of yeast growth.[30a] Biotin was isolated and crystallized as the methyl ester by Kögl and Tönnis in 1936 [31]; by painstaking effort they obtained 1.1 mg. of crystalline biotin from 250 Kg. of dried egg yolk. Preliminary studies of the chemical properties were made, but owing to the small amount of pure biotin available its chemical formula has not been elucidated. When du Vigneaud, Melville, György and Rose [32] injected Kögl's crystalline biotin methyl ester into rats suffering from egg white injury the dermatitis underwent involution, and the weight increased normally when daily doses as low as 0.1 microgram were administered.

That a characteristic dermatitis could be produced in experimental animals by feeding uncoagulated egg white was noted first during the period when there was widespread interest in the differentiation of the dermatitis-preventing factors in the vitamin B complex. Goldberger and Lillie [33] had produced in the rat a symmetric scaly dermatitis of the extremities and had referred to it as pellagra-like. Stimulated by the desire to identify the pellagra-preventive (P-P) factor, many investigators fed diets deficient in members of the vitamin B complex and produced a variety of cutaneous changes, which they termed pellagra-like. Natural foodstuffs were used as the sources of vitamins. Combined deficiencies and atypical cutaneous signs frequently resulted. Investigators in various parts of the world substituted certain foodstuffs in experimental rations, and previously described cutaneous lesions were

29. György, P.; Melville, D. B.; Burk, D., and du Vigneaud, V.: The Possible Identity of Vitamin H with Biotin and Coenzyme R, Science **91**:243 (March 8) 1940.

30. (*a*) Williams, R. J.: Growth Promoting Nutrilites for Yeasts, Biol. Rev. **16**:49 (Jan.) 1941. (*b*) West, P. M., and Wilson, P. W.: Biotin as a Growth Stimulant for the Root Nodule Bacteria, Enzymologia **8**:152, 1940.

31. Kögl, F., and Tönnis, B.: Darstellung von krystallisiertem Biotin aus Eigelb, Ztschr. f. physiol. Chem. **242**:43, 1936.

32. du Vigneaud, V.; Melville, D. B.; György, P., and Rose, C. S.: On the Identity of Vitamin H with Biotin, Science **92**:62 (July 19) 1940.

33. Goldberger, J., and Lillie, R. D.: A Note on an Experimental Pellagra-like Condition in the Albino Rat, Pub. Health Rep. **41**:1025 (May 28) 1926.

irregularly produced. The cutaneous signs of egg white injury were confused with those due to deficiencies of the vitamin B complex. Some investigators used egg white as a source of protein in diets designed to produce deficiencies of members of the vitamin B complex and thus further confused the subject. The majority of scaly dermatoses produced in the rat by nutritional means were broadly characterized as pellagra-like until György [15] clarified the differential diagnosis of the cutaneous changes due to egg white injury and those due to deficiencies of lactoflavin (riboflavin) and vitamin B_6 (pyridoxine). He recognized the vast possibilities of his elucidation and proposed a new approach in experimental dermatology based on the study of nutritional dermatoses in the rat. In collaboration with György at the Western Reserve University, one of us (M. S.) made a preliminary study of the gross and microscopic cutaneous changes due to egg white injury (vitamin H deficiency), lactoflavin (riboflavin) deficiency and vitamin B_6 (pyridoxine) deficiency.[34] This experiment was the starting point of the present series of investigations on nutritional dermatoses in the rat. The availability of crystalline vitamins has made it possible to plan nutritional experiments which approximate if they do not actually achieve uncomplicated single deficiencies. The scaly dermatoses produced by uncomplicated deficiencies of members of the vitamin B complex are characteristic and should not be confused with the cutaneous signs of egg white injury.[35]

EXPERIMENT

After consideration of the various diets which other investigators [36] used to produce the disease, it was decided to use a ration essentially similar to that employed in György's experiments.[15] The composition of the diet was as follows: dried commercial egg white,[37] 300 Gm.; Staley's corn starch, 177 Gm.; sucrose, 185 Gm.; McCollum salts 51, 58 Gm.[38]; peanut oil, 150 cc., and cod liver oil, 30 cc. The vitamin B

34. György, P.; Sullivan, M., and Karsner, H. T.: Nutritional Dermatoses in Rats, Proc. Soc. Exper. Biol. & Med. **37**:313 (Nov.) 1937.

35. Sullivan, M., and Nicholls, J.: (*a*) Nutritional Dermatoses in the Rat: I. Vitamin B_6 Deficiency, J. Invest. Dermat. **3**:317 (Aug.) 1940; (*b*) II. Skin Changes in Rats Deficient in the Entire Vitamin B Complex Other than Thiamin, ibid. **3**:337 (Aug.) 1940; (*c*) III. Gangrene and Spontaneous Amputation of the Digits Produced by the Combined Deficiency of Vitamin B_6 and the Filtrate Components, ibid. **4**:123 (April) 1941; (*d*) IV. Riboflavin Deficiency, ibid. **4**:181 (June) 1941; (*e*) VI. The Effect of Pantothenic Acid Deficiency, Arch. Dermat. & Syph., to be published.

36. Boas.[11] Friedberger.[12] Scheunert and Wagner.[13] Stenqvist.[14] György.[15] Parsons.[17] Salmon and Goodman.[21]

37. This was obtained from Weidman Co., Cleveland.

38. Adams, G., and McCollum, E. V.: A Method for the Biological Assay of Cod Liver Oil, J. Biol. Chem. **78**:495 (July) 1928.

complex was supplied as an alcoholic extract of brewers' yeast. One liter of 50 per cent alcohol was added to 100 Gm. of dried yeast [39] and stirred mechanically for two hours. The mixture was filtered and the filtrate evaporated to dryness on the starch before a fan at room temperature. In order to obtain a light homogeneous, palatable mixture, it was necessary to combine the dry ingredients of the diet separately and then add the oil slowly, mixing rapidly and thoroughly.

Young rats, each 18 days of age and weighing approximately 30 Gm., were selected and put into separate cages with raised screen floors. The

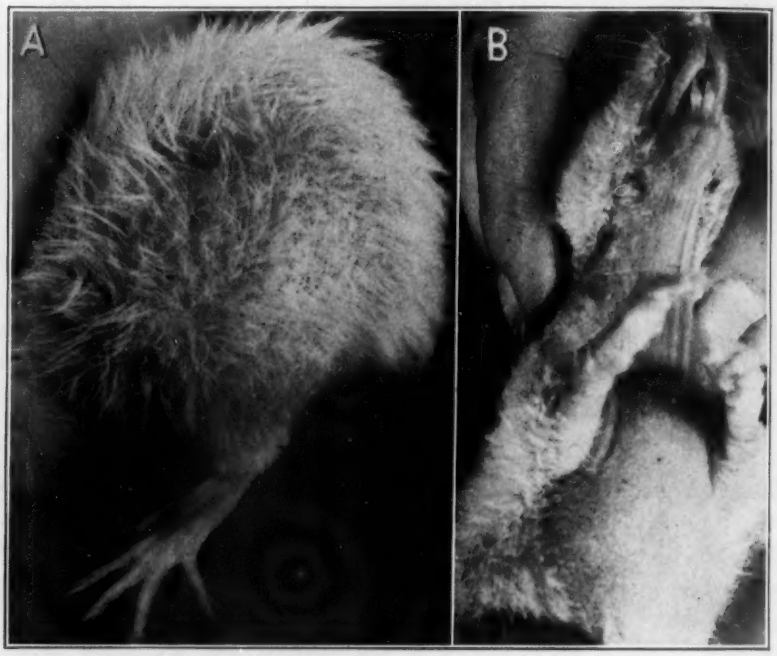

Fig. 1.—*A*, early scaling, brown crusts, diffuse alopecia and changes in the texture of the hair. *B*, erythema and edema of the lips and alopecia of the neck and abdomen.

diet was fed ad libitum in small-mouthed food cups which prevented the food from coming into contact with the body and minimized the chance of contamination of the food with excreta. During the course of the disease each rat consumed approximately 5 Gm. of food per day. Fresh food was frequently provided as the ration became moist on standing and adhered to the inflamed lips and eyelids of the rats, thus aggravating the dermatitis. A dilute solution of iodine was added to

39. Anheuser-Busch strain G.

the distilled drinking water once a week. The following signs and symptoms were observed in 125 animals:

During the first month there was a gain in weight of from 8 to 10 Gm. per week. The rats were lively and had excellent appetites. The onset of the cutaneous involvement varied from the third to the fifth week, depending on the initial weight and age of the rat. Usually the first sign was generalized erythema which was obscured by the fur. It was accompanied or followed by a rough appearance and loss of luster of the hair and generalized mild scaling. At first the scales were small, dry and white; later they were greasy and brown (fig. 1 *A*). Early in the disease the lower lips and the angles of the mouth were erythematous

Fig. 2.—Edema and erythema of the eyelids with sticky exudate on the margins resulting in adherence of the lids.

and edematous (fig. 1 *B*) and there were serous crusting and commissural fissuring. Later the upper lips were similarly involved. Next there was a symmetric alopecia, which often had its origin on the chin and the neck (fig. 1 *B*) and on the anterior portion of the venter. This extended either into the intertriginous region or onto the shoulders and the back of the neck, and then over and onto the head and snout. There was usually a simultaneous symmetric alopecia of the caudal portion of the venter which extended onto the outer aspect of the back of the thigh and also into the intertriginous regions. As a rule the alopecia spread rapidly in the aforementioned manner until only a few tufts of hair remained on the midportion of the flanks, the back and the head. However, there were variations in the usual pattern, and sometimes the

alopecia was asymmetric. In some animals there was generalized, diffuse, partial decrease in pigmentation of the fur. However, symmetric patterns of grayness similar to those associated with deficiencies of the vitamin B complex were never observed. At various periods after the onset of the cutaneous signs there was a sticky exudate on the inner canthi and on the margins of the eyelids, frequently causing them to adhere (fig. 2); however, when forced apart, the lids usually would not stick together again for several days. There were slight lacrimation

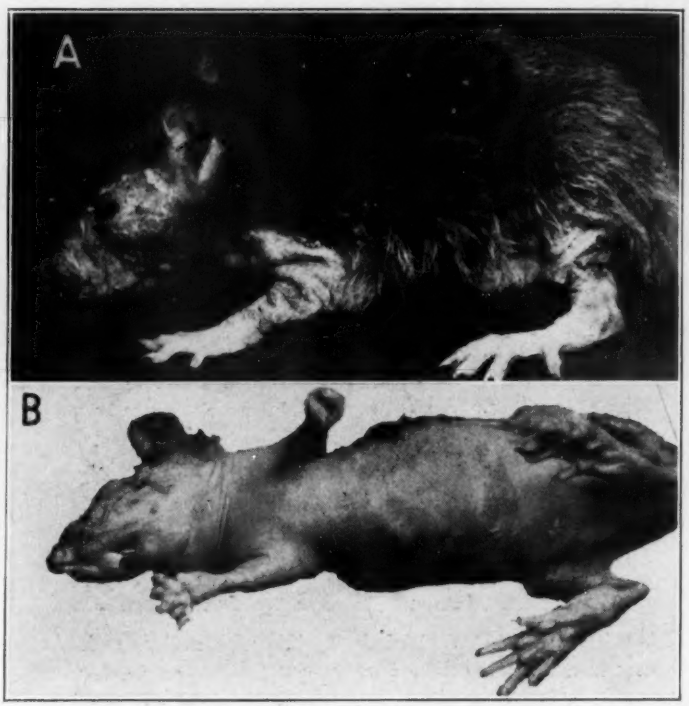

Fig. 3.—*A*, general appearance before complete loss of hair. Note desquamation and lichenification involving the skin of the face and extremities and also the matted appearance of the fur on the back. *B*, later stage showing smooth atrophic appearance of the skin.

and injection of the conjunctival vessels, but the corneas were clear. Occasionally there was some edema of the lids. During the course of the next several weeks scaly, erythematous and sometimes eczematous dermatitis involved the sides of the abdomen, the neck and the face (fig. 3 *A*). Brown crusting combined with fragmented hairs and fat piled high on the back and the few remaining hairs were matted together. Desquamation occurred in some areas, especially on the flanks and outer part of the thigh; following it the skin was either lichenified with

accentuation of the skin folds (fig. 3 *A*) or smooth and apparently atrophic (fig. 3 *B*). Finally the skin of every portion of the animal was affected (fig. 4 *A*) with the exception of the ears, the plantae and the middle and distal portions of the tail. In many animals there was a generalized exfoliation. There was never edema of the digits, and there was only a slight loss of hair on the dorsa of the paws after the generalization of the dermatitis in the late stage. Pruritus was exquisite and excoriations were frequent.

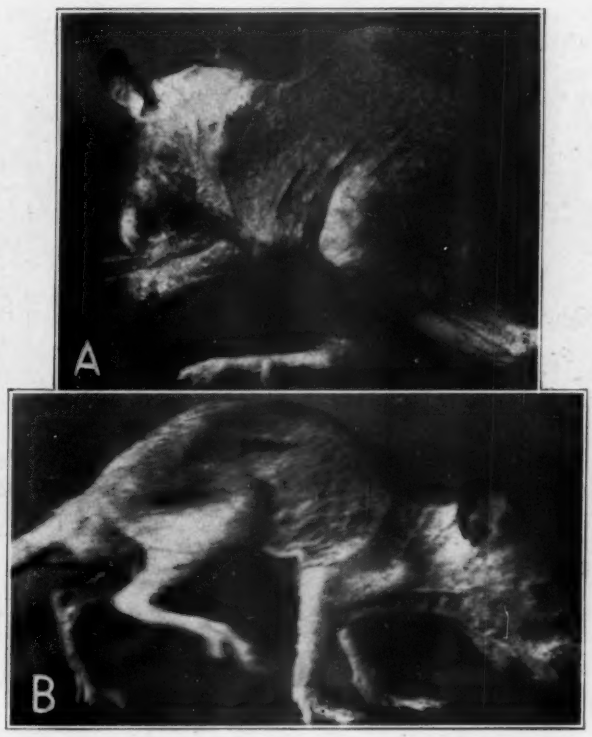

Fig. 4.—*A*, generalized exfoliation and brown crusting on the trunk. The ears, paws and tail are not involved. Note the characteristic humped position. There is exquisite pruritus at this stage. The rat is scratching the snout. *B*, abnormal gait.

As the disease progressed the appetite diminished. There were frequent attacks of diarrhea, and the animals were less lively. After several weeks of the disease they assumed a characteristic humped position (fig. 4 *A*). The caudal portion of the back was arched higher than the cephalic portion. There was a peculiar deliberate gait (fig. 4 *B*). When the rats attempted to move rapidly they hopped. They

were tense and hypertonic and jumped at the slightest noise or stimulation. Frequently there were tremors. The humped position and the abnormal gait persisted until death in the untreated rats. Keratomalacia was observed only in the late stage in a small percentage of the animals. Priapism occurred in about 50 per cent of the males.

The rats continued to gain weight for three or four weeks after the onset of the dermatitis; then the weight curves showed a plateau or a gradual decline until the death of the animals or until they were killed. It should be emphasized that the loss in weight usually followed the onset of the cutaneous signs. The animals usually survived for three to five months unless there was an intercurrent infection.

Fig. 5.—First stage showing moderate hyperkeratosis, acanthosis and slight diffuse infiltrate in the cutis.

HISTOLOGIC OBSERVATIONS

The earliest signs of alteration were moderate hyperkeratosis and uniform acanthosis (fig. 5), occasionally accompanied by a sparse, diffuse cellular infiltrate in the cutis. Next there were extensive hyperkeratosis, acanthosis and edema in the cutis. In some areas there was parakeratosis; in others, a serous exudate and extruded keratohyaline granules intermingled with the hyperkeratotic lamellas (fig. 6). Fragments of pigmented hair shafts were mixed with the crusts and the scales and contributed to the characteristic dark brown discoloration of the thick, greasy, material observed grossly and referred to by some

investigators[40] as pigmentation. In some sections there were small patchy areas of intraepidermal vesiculation. Edema in the upper part of the cutis occurred frequently and was occasionally accompanied by an increase in the cellular infiltrate and a few hyperemic and dilated blood vessels. Newly formed connective tissue was observed in the late stages in a few sections. There was no perifollicular or perivascular localization of the infiltrate. Endovasculitis was not observed. The sebaceous glands remained undisturbed during the early stages of inflammation. As the disease progressed the acanthosis was less uniform and patchy areas of thickened epidermis alternated with areas of approxi-

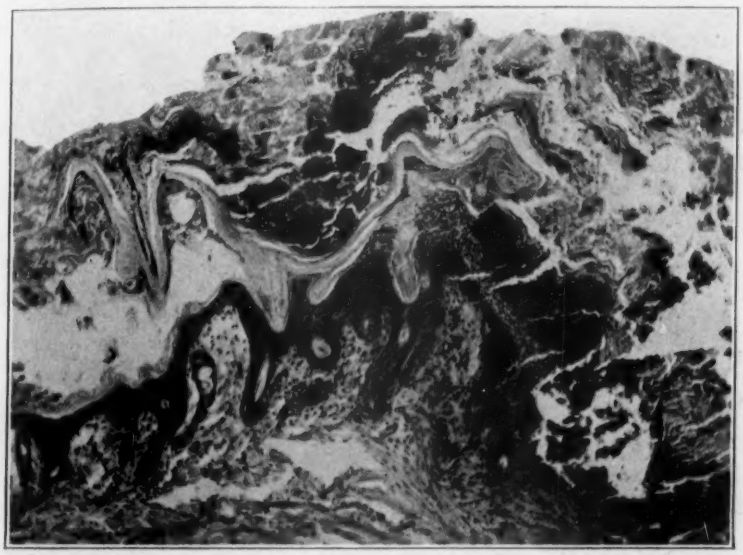

Fig. 6.—Stage showing extensive hyperkeratosis, parakeratosis and crusting.

mately normal thickness as well as atrophic areas. In the late stage there was a wide dilatation of the hair follicles, which resulted in an irregular finger-like or picket-fence-like formation of the epidermis (fig. 7 *A*). The abundant hyperkeratotic material plugged the gaping follicular orifices (fig. 7 *B*). In many sections the contrast of the tremendously thickened stratum corneum and the atrophic epidermis was striking. In some animals which survived many weeks there were a diminution in the size of the sebaceous glands and a disintegration of their cells. Small superficial epidermal abscesses and ulcerations were observed in a few sections. Small follicular abscesses were probably the result of infected excoriations. The meibomian glands and the rudimentary coil glands were not appreciably affected. Stainings for fat

40. Parsons,[17] Salmon and Goodman.[21]

during the course of the disease showed a normal distribution of sudanophilic material in the early stage. Later there were a decrease and then a disappearance of fat from the lower part of the cutis. There were abnormally large amounts of fat in the upper part of the epidermis. Throughout the various stages there was sudanophilic material in the region of the sebaceous glands (fig. 9).

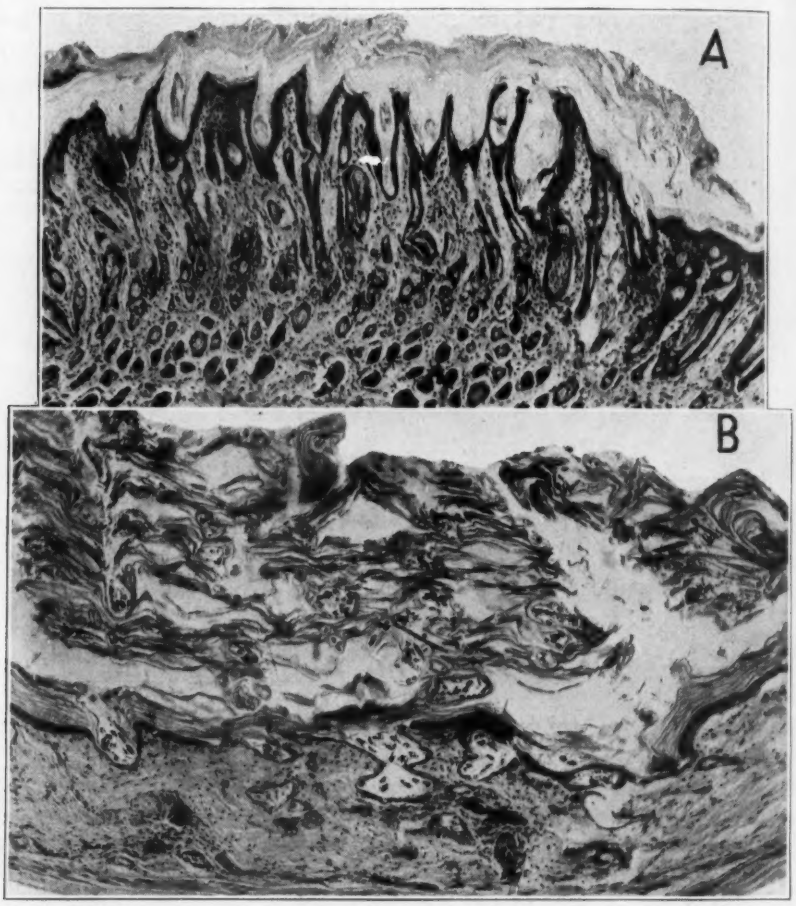

Fig. 7.—*A,* late stage showing hyperkeratosis and dilatation of some of the follicular orifices with resulting finger-like formation of the epidermis. *B,* final stage showing extensive hyperkeratosis and presence of numerous fragmented hair shafts. Note the contrast of the atrophic epidermis and the tremendous hyperkeratosis.

Administration of potent concentrates [41] of the protective substance was followed by immediate amelioration of all the signs and symptoms

41. Vitamin H concentrate, manufactured by I. G. Farbenindustrie. Biotin concentrate, manufactured by S. M. A. Co., Cleveland.

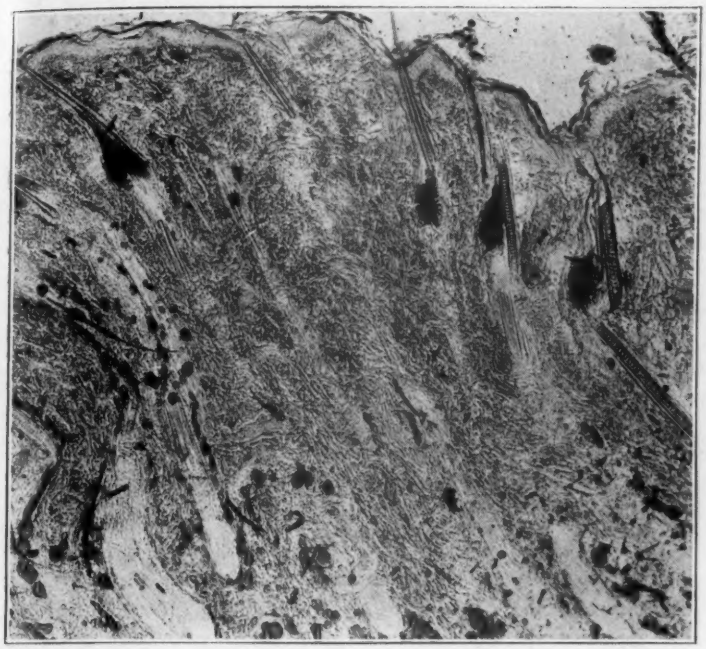

Fig. 8.—Skin of normal rat stained for fat, showing abundance of sudanophilic material in region of the sebaceous glands and in the lower part of the cutis. There is a barely detectable amount in the stratum corneum.

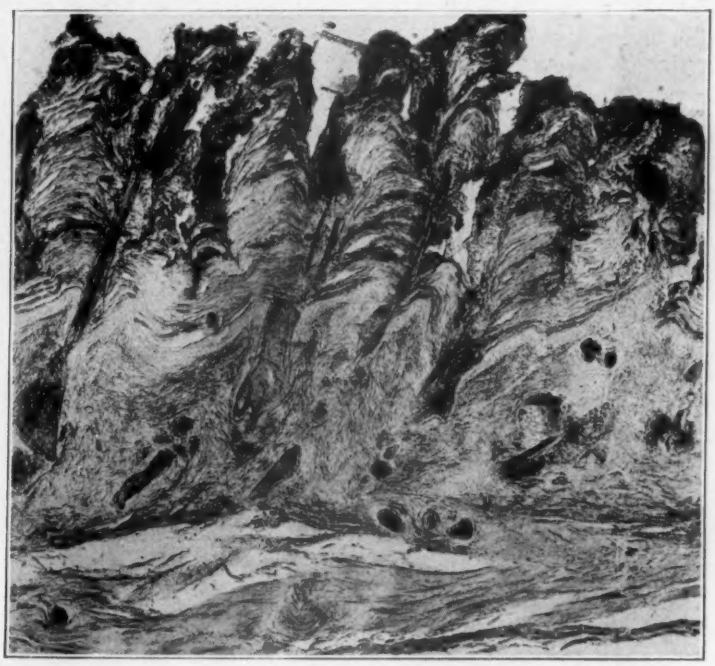

Fig. 9.—Skin of rat with extensive dermatitis stained for fat. Note the absence of fat in the lower part of the cutis and the tremendous amount in the region of the hyperkeratotic lamellas.

and a rapid gain in weight. Microscopic examination of the skin of animals after six weeks of treatment showed restitution to an approximately normal condition. There was no longer hyperkeratosis. The epidermis was slightly thinned or of an approximately normal thickness, and apparently new hair follicles were present. There was slight dilatation of the shafts of a few of the follicles. There was no cellular infiltrate in the cutis. The connective tissue was loosely arranged, and there was an abundance of fat in the lower part of the cutis.

COMMENT

In general, investigators [42] have described a characteristic lesion of the skin. Microscopic examinations have been made by only a few investigators.[43] With the exception of Millbradt,[44] the very brief reports of changes in the skin have been in general accordance.[45]

Success in the production of the disease depends on careful attention to several important details which influence the onset and severity of the lesion. Boas [11] emphasized the importance of the diet of the mother rat during pregnancy and found that the disease appeared sooner in the litters of undernourished mothers. Parsons [46] produced the disease more readily when the lactating mother was fed a diet containing uncooked egg white. Thus, the addition of egg white to the diet of the lactating mother or omission of foods containing the protective factor from the pregnant or lactating female hastens the appearance of the dermatitis in the young. However, it is unnecessary to modify the diet of the mother rat if sufficiently young stock rats are selected and weaned to the egg white diet. Boas [11] demonstrated that the initial weight of the rat was of importance. When young rats were used the cutaneous signs appeared within five to six weeks, whereas three months elapsed when adult rats were employed. György [16a] likewise pointed out the close correlation between the initial weight of the animal and the onset of cutaneous changes. The experience in this experiment has been in accord with the observations of Boas and György. Routinely rats

42. Boas.[11] Friedberger.[12] Scheunert and Wagner.[13] Stenqvist.[14] György.[15] Parsons.[17] Salmon and Goodman.[21] Findlay and Stern.[20]

43. (*a*) Friedberger, E., and Seidenberg, S.: Weitere Versuch über einseilige Ernährung mit Eiern, Deutsche med. Wchnschr. **53**:1507 (Sept. 2) 1927. (*b*) Scheunert, A.; Schieblich, M., and Wagner, E.: Weitere Untersuchen über die angebliche Unterwertigkeit gekochter Eier gegenüber Rohei, ibid. **54**:689 (April 27) 1928. (*c*) Falta and Noeggerath.[2] György.[15] Findlay and Stern.[20]

44. Millbradt, W.: Experimentelle Untersuchungen zur Frage der Bedeutung des H-Vitamins für die menschliche Pathologie, Dermat. Wchnschr. **103**:1376 (Oct. 10); 1402 (Oct. 17) 1936.

45. György.[15] György, Sullivan and Karsner.[34]

46. Parsons, H. T.: Personal communication to the authors.

18 days of age and weighing approximately 30 Gm. were used. It is possible but not practical to use smaller animals. When slightly older, heavier rats were employed by us, the disease either failed to appear or was delayed in onset and of a mild form. Some early investigators failed to observe dermatitis when they fed rats diets containing uncooked egg white. Analysis of their protocols shows that they almost invariably worked with adult rats. Rats apparently store the protective substance, and the onset of the dermatitis is delayed or prevented in the mature animals. Some investigators have observed that the disease is more readily produced at certain seasons.[47] In this experiment we observed that season had no effect on the production of the disease. In agreement with the observations of some investigators, we have noted that the disease appears earlier in male rats [48] and in albino rats.[49]

In order to evaluate the specific lesion of the disease, it is desirable to use a separate cage for each animal. Pruritus is a prominent symptom. When the dermatitis is widespread, the animal scratches, and there result excoriations, which sometimes become secondarily infected. By the single cage technic excoriations and injuries inflicted by cage mates are precluded, coprophagy is minimized and cannibalism is prevented.

The dietary ingredients must be carefully selected. Heating or denaturation of egg white destroys the injurious or disease-producing quality.[50] Therefore it is necessary to use either fresh raw egg white [51] or the commercial dried, powdered product.[52] It is more convenient to use the latter, but it is important to select a brand which has been dried at a low temperature (below 80 C.[18a]); inquiry should be made to the manufacturer concerning the drying temperature. The products of some firms are subjected to temperatures high enough to coagulate the egg white and remove its harmful properties.

The remainder of the diet must contain an adequate supply of all the aliments needed by the young rat to promote rapid growth and to assure the integrity of the skin. For example, our initial attempt to produce the disease failed when a commercial autolyzed yeast product was used as a source of the vitamin B complex. Failure again occurred when a yeast extract was prepared by a method which resulted in a

47. Friedberger and Seidenberg.[43a] Millbradt.[44]

48. Boas.[11] Parsons, Lease and Kelly.[18b] György.[16a]

49. Stenqvist.[14] Parsons, Lease and Kelly.[18b] György.[16a]

50. Fixsen, M. A. B.: The Effect of Desiccation upon the Nutritive Properties of Egg White, Biochem. J. **25**:595, 1931. Boas.[11] Scheunert and Wagner.[13] Stenqvist.[14] Parsons.[17] Parsons and Kelly.[18a]

51. Friedberger,[12] Scheunert and Wagner.[13] Stenqvist.[14] Parsons.[17]

52. Boas.[11] György.[15] Parsons.[17] Findlay and Stern.[20] Salmon and Goodman.[21] Friedberger and Seidenberg.[43a] Scheunert, Schieblich and Wagner.[43b]

product low in the vitamin B complex, as demonstrated by subsequent assay. In both instances no dermatitis was observed, and in from eight to ten weeks there was a rapid loss of weight followed by paralysis, typical of thiamine deficiency, and death. When additional thiamine was fed the paralysis was prevented, and when a potent yeast extract was substituted rapid growth was obtained and the disease produced. György [16a] encountered similar difficulties when he used cenovis and marmite as sources of the vitamin B complex. The method for yeast extraction which we found to be satisfactory was described by Mackenzie, Mackenzie and McCollum,[53] who maintained rats through several generations using the extract as the sole source of the complex.

The diet must not contain foodstuffs which are potent sources of biotin. Assay with rats and chicks showed that the protective factor was present in a wide variety of natural foods.[54] Originally we were under the impression that the diet in this experiment was devoid of biotin. However, microbiologic assay [55] revealed that the yeast extract contained 1 microgram of biotin per gram equivalent of yeast, the peanut oil contained 0.004 microgram per gram and the starch and sugar each had less than 0.00025 microgram per gram. On the basis of the average daily consumption of 5 Gm. of food per rat, the daily intake of biotin was at least 0.555 micrograms. Parsons and Kelly [18j] showed that the requirement for the protective factor was proportional to the amount of egg white in the diet. Eakin, Snell and Williams,[56] using yeast, reported a quantitative relation between biotin and a biotin-inactivating factor isolated from raw egg white. It is likely that a similar inactivation of biotin causes egg white injury in animals. The biotin in the diet probably is bound or blocked by the substance in egg white and is unavailable to the animal. Thus the disease is prevented or cured only by the administration of additional amounts of biotin. György, Rose, Eakin, Snell and Williams [57] have recently presented evidence to support this theory. The biotin requirement of the rat is unknown. Therefore in order to produce the disease with certainty it is advisable to use large amounts of egg white.

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53. Mackenzie, C. G.; Mackenzie, J. B., and McCollum, E. V.: Growth and Reproduction on a Low Fat Diet, Biochem. J. **33**:939 (June) 1939.

54. Boas.[11] György.[15] György.[16a] Parsons and Lease.[18e]

55. These assays were made by Dr. H. J. Prebluda, Research Development Laboratory, U. S. Industrial Chemicals Inc., Baltimore.

56. Eakin, R. E.; Snell, E. E., and Williams, R. J.: A Constituent of Raw Egg White Capable of Inactivating Biotin in Vitro, J. Biol. Chem. **136**:801 (Dec.) 1940.

57. György, P.; Rose, C. S.; Eakin, R. E.; Snell, E. E., and Williams, R. J.: Egg White Injury as the Result of Non-Absorption or Inactivation of Biotin, Science **93**:477 (May 16) 1941.

SUMMARY

When a diet containing unheated and uncoagulated commercial dried egg white as the source of protein was fed to young rats a characteristic dermatosis was produced.

The cardinal features of the disease were a generalized, symmetric, erythematous, scaly, greasy, pruritic dermatitis, poor growth and an abnormal posture and gait in the late stages.

Microscopically there were extensive hyperkeratosis, some parakeratosis, acanthosis and edema. Broken hair shafts and serous crusts were intermingled with the hyperkeratotic lamellas. There was dilatation of the follicular shafts, and the patulous orifices were plugged with hyperkeratotic material. In the late stage of the disease there was some atrophy of the epidermis, which contrasted with the abundant hyperkeratosis. There was an excessive amount of sudanophilic fat in the hyperkeratotic lamellas.

The administration of the protective substance, biotin, in the form of crude concentrates resulted in the restitution of the integrity of the skin, as judged by gross and microscopic inspection.

A technic for the production of this experimental disease is described. Attention to details concerning the selection of suitable animals and the choice of appropriate food materials is of utmost importance for the successful production of the disease.

ABSTRACT OF DISCUSSION

Dr. Paul György, Cleveland: I feel honored in having the opportunity to discuss this excellent paper and am particularly pleased in that the egg Dr. Sullivan and I laid six years ago in joint work in Cleveland developed to a full-fledged chick without any sign of egg white injury. I feel even that the chick is almost a hen that can now and does lay eggs without any further help.

Egg white injury is an exceedingly interesting problem and is a new principle in the production of disease, and not only disease of the deficiency type. As the authors have pointed out, the most probable explanation for egg white injury is that egg white contains a substance which makes the protective and corrective factor called biotin unavailable for the organism. It has been shown recently that the protein-like substance from egg white can be isolated and that it is contained in very low concentration, about 10 micrograms in 1 cc. of fresh egg white. This substance is now called avidin. The term is derived from "avid" and denotes a hungry substance. When egg white and biotin are eaten at the same time, the avidin binds the biotin and inactivates it by forming a compound which cannot be digested and which is excreted with the feces. Thus a deficiency disease is produced in the intestine, although the supply of the corresponding vitamin is large enough to protect the organism provided no avidin is present in the diet.

As a medical man I drew the theoretic conclusion that a substance that is so active must have great importance for life. In Mammalia, in rats and in all other mammals and probably in man, biotin deficiency can be produced, at least at present, only by a diet that contains egg white. In chicks it has now been

shown definitely that biotin deficiency can be produced by a synthetic diet that is free from biotin and egg white. The analogy between vitamin K and biotin is obvious. The chick is almost the only animal species in which vitamin K deficiency can be produced, whereas in Mammalia some other factor is needed, such as the ligation of the bile duct or jaundice (in man) in order to produce a vitamin K deficiency. My assumption is that Mammalia can produce biotin in the intestinal flora and that the supply of biotin thus produced is probably sufficient, but that is only an assumption and has to be proved.

DR. PAUL GROSS, New York: I believe that the dermatologic profession should express its thanks to Dr. Sullivan and his collaborator, since definite benefit to dermatology will eventually be derived from the histologic studies of the cutaneous diseases of the rat caused by the various deficiencies of the vitamin B complex. The egg white damage of the rat as presented by Dr. Sullivan and his collaborator is of broad interest to the dermatologist, since it produces an extensive dermatosis which has been compared to seborrheic dermatitis of man. It demonstrates a mechanism in which I have been greatly interested in connection with metal poisoning. In a paper read a few days ago, my collaborators and I demonstrated that chronic zinc chloride poisoning produces a clinical syndrome in the rat which can be identified with pantothenic acid deficiency. In both instances vitamin deficiency became manifest as a result of feeding of a substance in toxic amounts. Another example of this mechanism can be found in the experimental selenium poisoning of the rat and the spontaneous disease in cattle produced by seleniferous food. The clinical manifestations of selenium poisoning of the cattle bear such a resemblance to human pellagra that Barondes speculated on the possibility that pellagra might be due to seleniferous food. Of course, this was before the fundamental discovery of nicotinic acid as a pellagra-preventive factor. Recent studies on the synthesis of various members of the vitamin B complex in the rumen explain why manifestations of vitamin deficiencies do not develop in cattle. It is therefore possible that the disease observed in cattle is a vitamin deficiency precipitated by selenium poisoning, just as the egg white damage represents the biotin deficiency of the rat, which never occurs spontaneously in this animal.

DR. MAURICE SULLIVAN, Baltimore: This disease was brought to attention at this meeting because much will be heard about biotin within the next few years. Biotin is a well known yeast neutrilite, or growth factor, of the bios group. As Dr. György has emphasized, extraordinarily small amounts of it are present in the richest natural sources. Biotin was isolated and crystallized as the methyl ester by Kögl and Tönnis in 1936. They were able to obtain only 1.1 mg. of crystalline biotin from 250 Kg. of dried egg yolk. Preliminary studies of the chemical properties of biotin have been made, but the exact chemical formula has not yet been elucidated.

FIBROTIC NODULES OF THE SKIN

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AND
L. H. WINER, M.D.
MINNEAPOLIS

The peculiar ability of the skin to form fibrous tissue and its accumulation in fibrous nodules led us to study the various conditions in which such changes occur and endeavor to find the reason for their occurrence. Nodules appear after trauma and with such general systemic diseases as syphilis, yaws, leprosy, scleroderma, rheumatic fever, rheumatoid arthritis and acrodermatitis chronica atrophicans. Fibrous tissue is also seen in the harmless subepidermal fibrosis and in a fibrous accumulation over the knuckles called knuckle pads.

What causes this fibrous reaction? Why do the nodules so often occur over joints? Why do they occur with systemic diseases? Are there any clinical and histologic differences in the various lesions? Can long-continued oft repeated slight trauma be the only causative factor or is there a fibrotic diathesis in persons who have these lesions?

Juxta-articular nodes are found in both syphilis and yaws. They were first described by the Brazilian physician Adolph Lutz [1] in 1891. Jeanselme [2] in 1889, MacGregor [3] in 1900 and Steiner [4] in 1904 all described the disease independently from studies in different tropical regions. Jeanselme had given it the name *nodosités juxta-articulaires* in 1900. All of these early investigators believed that it was due to yaws and considered it a tropical disease until 1918, when Sellei [5] reported

From the Department of Dermatology and Syphilology, University of Minnesota, Dr. H. E. Michelson, Director, and the Department of Dermatology and Syphilology, Minneapolis General Hospital, Dr. S. E. Sweitzer, Chief.

1. Lutz, A.: Correspondence—Letter of Dr. A. Lutz, written in September 1891, Monatsh. f. prakt. Dermat. **14**:30-34, 1892.

2. Jeanselme, E., cited by Hoffmann, H., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 12, pt. 1, pp. 419-498.

3. MacGregor, W.: An Address on Some Problems of Tropical Medicine, Lancet **2**:1055-1061, 1900.

4. Steiner, L.: Ueber multiple subcutane, harte fibrose Geschwülste bei den Malayen, Arch. f. Schiffs- u. Tropen-Hyg. **8**:156-159, 1904.

5. Sellei, J.: Tumor fibrosus syphiliticus, Gyógyászat **25**:25, 1918; abstracted, Dermat. Wchnschr. **74**:485, 1922.

several cases from Bosnia. In 1920 de Quervain [6] noted the condition in a Swiss who had never left his birthplace. Sellei, although he did not know of the relation of his cases to those of Jeanselme, did establish syphilis as the cause of his cases. Jessner [7] inoculated a portion of a nodule into a rabbit, in which syphilis subsequently developed. Recently Aravijskij and Bulvachter [8] reported finding spirochetes in the nodule of a Siberian peasant who had syphilis.

Juxta-articular nodes are usually located on the extensor surfaces but occasionally may be found on the flexor surfaces of the joints. The most frequent site is the extensor surface of the elbow, and the next most frequent, the extensor surface of the knee. The feet, hips, forearms, hands, fingers, ribs, shins, ear region, thighs and forehead have also been reported as sites. The lesions are usually multiple hard round or egg-shaped nodules varying in size up to that of a hen's egg. The skin over the nodules may be normal or reddened. Occasionally they break down.

Histologically, in accord with the observations of Jeanselme, the node divides itself into three zones: an outer zone of inflammatory changed connective tissue, a narrow middle zone consisting of partly degenerated connective tissue, poor in nuclei, and a central zone of hyaline degenerated tissue and amorphous masses with interspersed nuclear rests.

Practically all writers consider mild trauma continuously repeated a necessary cause of the nodules. If not the only cause, trauma is always contributory. Most of these nodules slowly disappear under antisyphilitic therapy. Two of our patients were refractory to treatment; one of them was a nonsyphilitic person in whom the lesions were due to trauma.

Subcutaneous nodular formations have been frequently noted in the rheumatic group of diseases. Coates and Coombes [9] reported that the histologic formation of nodules of rheumatoid arthritis, Still's disease and endocarditis lenta are histologically the same as those of orthodox rheumatic infections. Dawson and Boots,[10] Swift [11] and Klinge and Grzi-

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6. de Quervain, F.: Multiple juxta-artikulare fibrose-gummose Knoten, Schweiz. med. Wchnschr. **50**:629, 1920.

7. Jessner, M.: Luetische juxta-artikulare Knotenbildungen, Zentralbl. f. Haut- u. Geschlechtskr. **38**:433, 1931.

8. Aravijskij, A., and Bulvachter, A.: Zur Frage der symbiotischen Infektion bei syphilitischen juxtaartikularen Verhartungen, abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **39**:443-444, 1931-1932.

9. Coates, V., and Coombes, C. F.: Observations on the Rheumatic Nodule, Arch. Dis. Childhood **1**:183-193, 1926.

10. Dawson, M. H., and Boots, R. H.: Subcutaneous Nodules in Rheumatoid (Chronic Infectious) Arthritis, J. A. M. A. **95**:1894-1896 (Dec. 20) 1930.

11. Swift, H.: Rheumatic Fever: Hektoen Lecture, Billings Foundation, J. A. M. A. **92**:2071-2083 (June 22) 1929.

Fig. 1.—Juxta-articular nodes on the elbow in a patient with syphilis.

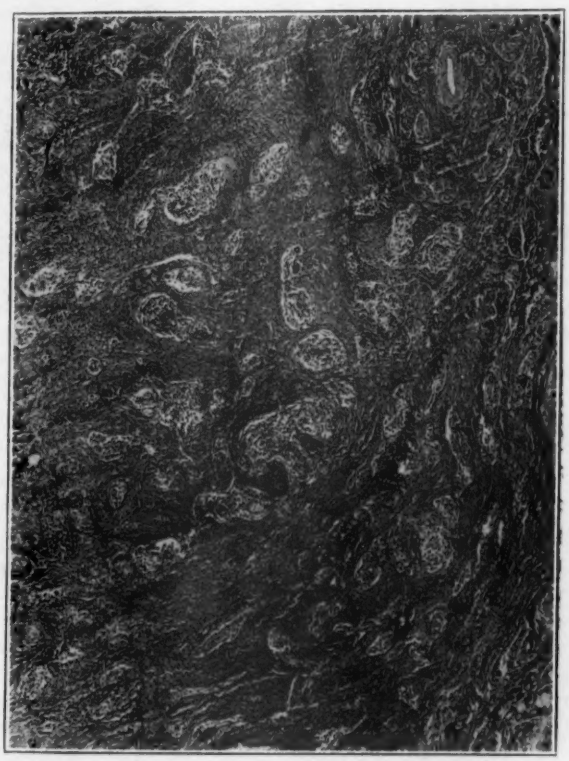

Fig. 2.—Photomicrograph (× 36) of a section through a syphilitic juxta-articular node. Note the vascular involvement.

mek [12] agreed that rheumatic fever and rheumatoid arthritis are different manifestations of the same fundamental process. Twenty per cent of patients with rheumatoid arthritis have nodules. The nodules vary in size from 1 cm. in diameter to the size of large olives. The site most frequently involved is the extensor surface of the forearm at a point about 4 cm. distal to the olecranon. The areas next most frequently involved are the region directly over the oleocranon, the dorsum of the forearm, the hand, the knee, the sacral region and the scalp. The nodules are moderately firm, always discrete and located in the subcutaneous tissue. They are attached to neither the skin nor the underlying periosteum; however, they frequently show a relation to tendon sheaths and the walls of bursae. Their development is slow, and they persist for a number of years. The smaller nodules have been known to develop and disappear in a few months. Only in rare instances do these nodules cause pain.

The histologic structure was described in detail by Dawson and Boots. Collins [13] explained that the variation in histologic structure was due to variation in the age of the nodules studied. The nodules histologically show a central area of necrosis surrounded by a middle zone of large mononuclear cells which are arranged in palisade formation or radially around the central necrotic zone. A peripheral zone consisting of dense vascular connective tissue encloses the entire node. There are endothelial hyperplasia and a subendothelial deposit of fibrin in the arterioles and capillaries. Narrowing occlusion of the lumen and in some instances canalization of hyperplastic intima, polypoid projections into the lumen, splitting of the elastica and the formation of a new internal elastic coat are frequently noted. A perivascular infiltrate of mononuclear and small round cells is present. All rheumatic nodules have this characteristic histologic structure, which shows no relation to the subcutaneous nodes encountered in syphilis, gout or any chronic granuloma. Schosnig [14] stated that in rheumatic nodules the fibrous tissue simply undergoes solution, whereas in fibrous gumma, tuberculosis or phlegmon the fibrillary necrosis results in caseation.

Oppenheim [15] cited Herxheimer as having demonstrated the first case in which the association of acrodermatitis chronica atrophicans with fibrotic nodules was noted. In the discussion of his first case in 1907,

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12. Klinge, F., and Grzimek, N.: Das Gewebsbild des fieberhaften Rheumatismus, Virchows Arch. f. path. Anat. **284**:646-711, 1932.

13. Collins, D. H.: The Subcutaneous Nodule of Rheumatoid Arthritis, J. Path. & Bact. **45**:97-115, 1937.

14. Schosnig, F.: Das Gewebsbild des fieberhaften Rheumatismus, Virchows Arch. f. path. Anat. **286**:291-302, 1932.

15. Oppenheim, M., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 8, pt. 2, p. 574.

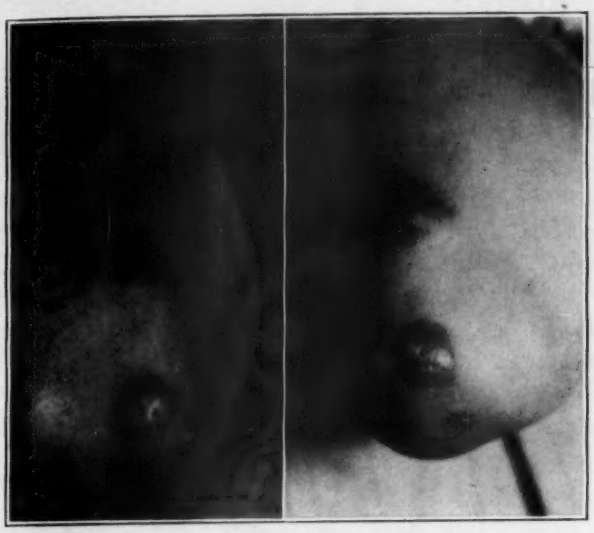

Fig. 3.—Traumatic juxta-articular nodes on the elbows of a nonsyphilitic machinist.

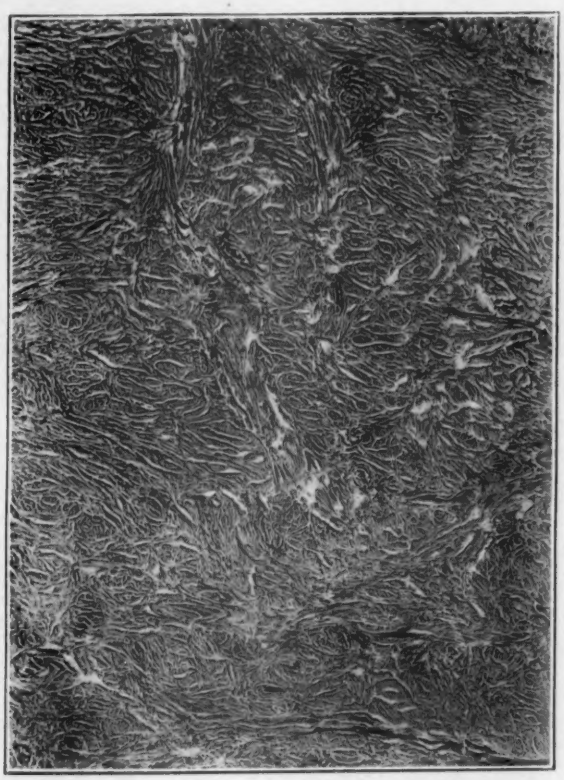

Fig. 4.—Photomicrograph (× 36) of a section through a traumatic juxta-articular node. Note the dense fibrosis and the almost complete absence of cellular infiltrate.

Oppenheim [16] stated that there is a relation in the association of the two conditions and that owing to the loss of elastic fibrils the collagenous fibers may proliferate and grow unlimitedly. At present these nodules are considered as a final phase of acrodermatitis chronica atrophicans, namely, the hypertrophic fibrous stage. The sites involved are the knees, elbows, dorsa of the hands and occasionally other regions, the elbows being most frequently involved. The nodes are painless, are single or multiple and vary in size from 0.5 to 2 cm. in diameter. The color varies from white or yellow to cyanotic red. Nobl [17] called the lesions pseudofibromatoses, as did Goldschlag.[18] Histologically they consist of hypertrophic collagenous fibers in which the elastic fibrils are entirely absent.

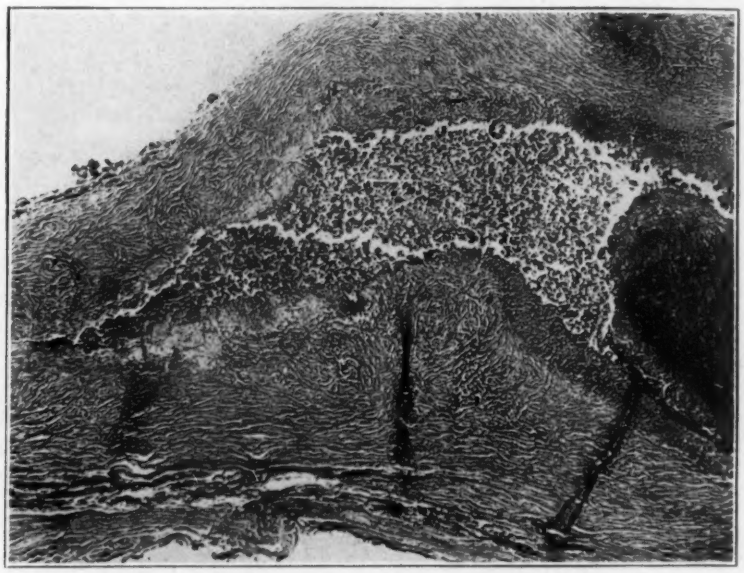

Fig. 5.—Photomicrograph (× 36) of a section through a rheumatic nodule, showing central necrosis and peripheral fibrosis.

There is a dense infiltrate of plasma and round cells surrounding the hyperplastic collagen.

Fibrotic nodules are much less common in scleroderma than in acrodermatitis chronica atrophicans. Lipschutz,[19] Fletcher [20] and Gray [21] all

16. Oppenheim, M.: Arch. f. Dermat. u. Syph. **88**:145, 1907.

17. Nobl, G.: Pseudofibromatose bei Akrodermatitis atrophicans, Zentralbl. f. Haut- u. Geschlechtskr. **13**:37, 1924.

18. Goldschlag, F.: Acrodermatitis Atrophicans with So-Called Pseudofibromas, Zentralbl. f. Haut- u. Geschlechtskr. **27**:593, 1928.

19. Lipschutz, B.: Knotenformige Hautverdeckungen bei Sklerodaktylie, Dermat. Wchnschr. **57**:851-857, 1913.

described fibrous nodules in cases of scleroderma with sclerodactylia. These nodules were located on the extensor surfaces of the fingers and varied in size from 0.25 to 0.5 cm. in diameter. The color of such nodules is that of the overlying skin, and they are firmly attached to both the skin above and the underlying joint capsule or muscle below. Histologically, the nodes consist of hyperplastic hyalinized collagenous fibrils, in the midst of which are blood vessels in which the endothelium is proliferated. The vessels are surrounded by a closely packed infiltrate of round cells. The periphery of the nodule is limited by a round cell infiltrate. The elastic fibers, although fragmented, are present.

Nodular subepidermal fibroses of Michelson,[22] although not a subject of voluminous literature, are of frequent clinical occurrence. Subepidermal fibrosis is an entity synonymous with fibroma simplex of Unna,[23] dermatofibroma of Traub and Monash,[24] dermatofibroma lenticulare of Schreus [25] and noduli cutanei of Arning and Lewandowsky.[26] They may be single or multiple and are located mostly on the extremities but do not favor the region of joints. The favorite sites are the extensor surfaces of the tibia and forearms, but any part of the body may be involved. They are small hard flat lesions like shots buried superficially in the integument. They vary from 0.5 to 3 cm. in diameter, and their color varies from red to dull brown, depending on their age. The lesions are painless, are not tender and do not itch. Cauterization or excision removes the lesions and they show no tendency to recur. We have studied sections from numerous cases for the past several years and histologically have observed in all of them a circumscribed proliferation of the collagenous fibrils in the deep reticular cutis. The interfascicular spaces are compressed, obliterating the lymph spaces. Sebaceous glands are absent, and sweat glands below the involved area are atrophic or compressed. Histologically the lesion is stellate and contains few vessels in its substance. The periphery, although not encap-

20. Fletcher, H. M.: Sclerodermia and Sclerodactylia, Proc. Roy. Soc. Med. **14**:40-41, 1920-1921.

21. Gray, A. M. H.: Generalized Sclerodermia with Subcutaneous Nodules, Proc. Roy. Soc. Med. **16**:107-108, 1922-1923.

22. Michelson, H. E.: Nodular Subepidermal Fibrosis, Arch. Dermat. & Syph. **27**:812-820 (May) 1933.

23. Unna, P. G.: The Histopathology of Diseases of the Skin, translated by N. Walker, New York, Macmillan & Co., 1896, p. 836.

24. Traub, E. F., and Monash, S.: Dermatofibroma, Arch. Dermat. & Syph. **26**:250 (Aug.) 1932.

25. Schreus, H. T.: Dermatofibroma lenticulare, Fibroma simplex (Unna), Noduli cutanei (Arning und Lewandowsky), Arch. f. Dermat. u. Syph. **161**:456-461, 1930.

26. Arning, E., and Lewandowsky, F.: Noduli cutanei; eine bisher wenig beobachtete Hautaffektion, Arch. f. Dermat. u. Syph. **110**:3-14, 1911.

Fig. 6.—Fibrotic nodes on the elbow of a patient with acrodermatitis chronica atrophicans.

Fig. 7.—Photomicrograph (× 75) of a section through a fibrotic node in a case of acrodermatitis chronica atrophicans. Note the prominence of the hyperplastic collagen in the middle and lower parts of the cutis.

sulated, stands sharply in contrast with the normal connective tissue which circumscribes it. At the junction of the normal and abnormal tissues the blood vessels show marked sclerosis. The elastic tissue within the lesion is greatly diminished or entirely absent. One is impressed, except for the irregularity, by the similarity to a true scar. Michelson considered these lesions a response of the connective tissue to a low grade excitant which does not bring about suppuration or liquefaction but results rather in scar formation similar to keloid. Since Senear and Caro [27] considered this condition as possibly a histiocytoma, we have studied frozen sections using stains for fat and injected saccharated iron, 1 per cent, into lesions. We have been unable to note any excessive presence of fat or iron granules in phagocytic cells, as mentioned by Senear and Caro, and can agree with Stecker and Robinson [28] that the histiocytes reported are probably wandering phagocytes and that the tumor itself is not a histiocytoma.

Wise presented a case of juxta-articular nodes [29] located on the elbows of a leper at a meeting of the New York Dermatological Society in October 1939, and the histologic picture of the nodules was consistent with the diagnosis of leprosy. He presented the same case on April 23, 1940, at which time the nodules had diminished greatly in size after injections of chaulmoogra oil and the other cutaneous lesions had partly cleared up.

Associated with juxta-articular nodes of leprosy is either the neural form of leprosy or nodular leprosy of the eyebrows, ears, face and hands. Verification can be made by the finding of lepra bacilli in nasal smears or in a biopsy specimen of the node or of the ulnar nerve. Histologically, in the late stages the node shows central caseation. In the early stages the node consists of fibroblastic central reaction in the cutis and subcutis and vessel wall proliferation. Nests of small lymphocytes together with a few plasma cells are located on the periphery of the node. The greater portion of the infiltrate consists of epithelioid cells, many of which are multinucleated Langhans giant cells.

Tuberculous juxta-articular nodes are frequently associated with a tuberculous joint and are usually of the colliquative type. Clinically, early in their course, their appearance is that of firm subcutaneous nodes attached to the underlying bone or bursa. Within two or three weeks they grow larger, soften in the center and have the appearance of a

27. Senear, F. E., and Caro, M. R.: Histiocytoma Cutis, Arch. Dermat. & Syph. **33**:209-226 (Feb.) 1936.

28. Stecker, J. F., and Robinson, W. L.: Dermatofibroma, Arch. Dermat. & Syph. **43**:498-503 (March) 1941.

29. Wise, F.: (*a*) Leprosy with Juxta-Articular Nodes, Arch. Dermat. & Syph. **41**:789 (April) 1940; (*b*) **42**:1162 (Dec.) 1940.

"cold abscess," which breaks through the skin by means of multiple sinuses and exudes a relatively scanty amount of pus for the size of the lesion. A positive reaction to a tuberculin test, the histologic observation of liquefaction necrosis surrounded by tubercle formation and the presence of tubercle bacilli both in the secretion from the sinuses and in the tissue are definite stigmas of tuberculous pathogenesis.

Garrod [30] in 1893 reported an unusual form of nodules on the joints of the fingers in 3 patients and in 1904 reported 12 other cases of the condition. White,[31] Jones,[32] Hauck,[33] Moncorps,[34] Weber [35] and Krantz [36] all have subsequently written on this condition. Several cases have been reported under the designation of knuckle pads, and this seems to us to be a good name for the condition. The lesions are found on the extensor surfaces of the fingers but not on the thumbs. They are located over the proximal interphalangeal joints, centrally and also to one side of the joint. They feel as if something firm had been deposited under the skin and give the impression of connective tissue thickening. They are freely movable over the joint but are firmly attached to the overlying skin. They vary in size from 3 to 15 mm. in diameter. The skin over the nodules looks hyperkeratotic. Usually there are no subjective symptoms, but occasionally the patient complains of some pain. The roentgen examination of the bones and joints shows no pathologic changes. The lesions may appear at any age but are permanent. When multiple they do not appear simultaneously but develop at intervals. In about half the cases observed the nodules have been associated with Dupuytren's contraction, either in the patient himself or in the parents. In later life many are associated with camptodactylia (little finger bent clawlike). In most cases there is no history of trauma. Histologically, Hauck considered the condition a true fibroma. In the cases which we studied microscopically there was increased fibrous connective tissue in the deep part of the cutis. The elastic tissue in the upper part of the cutis was normal, but it was absent in the area where the connective

30. Garrod, A. E.: (*a*) On an Unusual Form of Nodule upon the Joints of the Fingers, St. Barth. Hosp. Rep. **29**:157-161, 1893; (*b*) Concerning Pads upon the Finger Joints and Their Clinical Relationships, Brit. M. J. **2**:8, 1904.

31. White, W. H.: On Pads on the Finger Joints, Quart. J. Med. **1**:479-480, 1907-1908.

32. Jones, H. W.: Two Cases of Knuckle Pads, Brit. M. J. **1**:759, 1923.

33. Hauck, G.: Ueber subcutane Fibrome an der Dorsalseite der Fingermittelgelenke, Med. Klin. **20**:1569, 1924.

34. Moncorps, C.: Keratosis supracapitularis seu pulvinata, Zentralbl. f. Haut- u. Geschlechtskr. **54**:291, 1936.

35. Weber, F. P.: A Note on Dupuytren's Contraction, Camptodactylia and Knuckle Pads, Brit. J. Dermat. **50**:26-31, 1938.

36. Krantz, W.: Ueber die "Fingerknöchelpolster" ("Knuckle-Pads"), Dermat. Wchnschr. **107**:945-949, 1938.

tissue was increased. The epidermis was unaltered except for great thickening of the stratum corneum. No cellular infiltrate or inflammatory change of any type was in evidence.

Clinically, knuckle pads are to be differentiated from Heberden's nodes, gouty nodules, synovial lesions and glomus tumors. Heberden's nodes occur at the distal interphalangeal joints and are firmly attached to the bone. Gouty nodules show the presence of uric acid crystals. Synovial lesions are located anywhere between the terminal interphalangeal joint and the root of the nail and are cystic or soft. The glomus

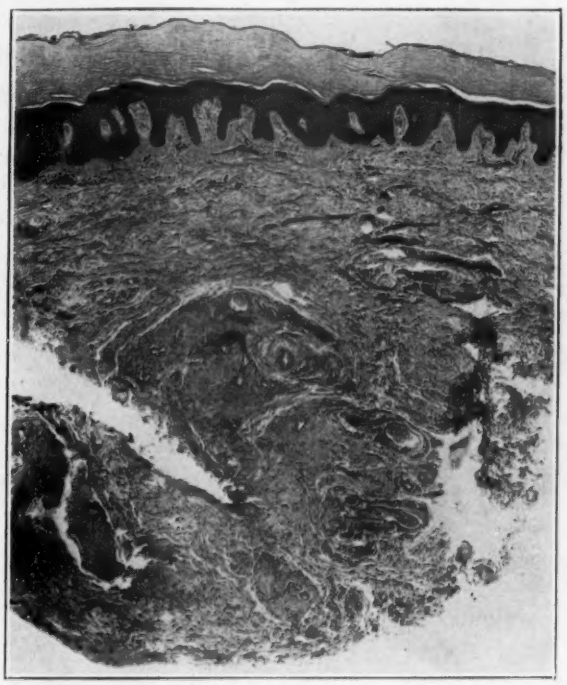

Fig. 8.—Photomicrograph (× 36) of a section through a knuckle pad. Note the fibrosis in the deep part of the cutis.

tumor is characterized, usually, as being a painful tumor under the finger nail. Weidman and Wise [37] reported a case of multiple glomus tumors which were not painful and were not located under the nails. Histologically, a glomus tumor is a hamartoma of the arterial system and is usually surrounded by well organized nerve tissue and epithelioid cells.

In an examination of these various fibrous lesions we have arrived at the conclusion that oft repeated slight trauma is a large factor in their

37. Weidman, F. D., and Wise, F.: Multiple Glomus Tumors of the Order of Telangiectases, Arch. Dermat. & Syph. **35**:414-424 (March) 1937.

causation but not the only factor, as they are found in areas where trauma seldom occurs. Weiss [38] has shown in tissue culture that tension causes fibroblasts to multiply. This mechanical stimulus not only causes increase in fibroblasts but determines their direction of deposition, namely, parallel to the line of stress.

Cowdry [39] stated that with some injuries the epithelium suffers as a result of nutritional deficiency, but occasionally the connective tissue, whose nutritional needs are less, is unaffected and may increase. This phenomenon, known as fibrosis, is manifested by multiplication of fibroblasts and formation of additional fibers. Fibrosis can also be explained by the fact that fibroblasts are believed by some cytologists to be generalized cells (not specialized) which retain the ability to proliferate and multiply when injured. This property has been lost by the epithelial cells, which are more highly specialized.

Jordan [40] stated the beliefs that regeneration of destroyed connective tissue cells calls forth embryonal connective tissue and that fibroblasts increase by cell division. Loose connective tissue is a direct descendant of mesenchyme. Fibroblasts, or their descendants, occur wherever mesenchyme makes its way, which is almost everywhere. Clark [41] expressed the belief that the increased numbers of fibroblasts were derived from proliferating mitotic histiocytes in inflammatory foci. Aykroyd and Zuckerman [42] determined that fibroblasts controlled the regional distribution of body fluids in the connective tissues of the body. The tissue fluid which surrounds the fibroblasts is relatively stagnant in that it does not circulate as rapidly as the blood circulates. It is therefore plausible that at any place in the body where the tissue fluids become stagnant from disease or injury, the response can be a proliferation of fibroblasts and finally the formation of fibrosis.

In our experience with various kinds of fibrosis, we found no associated hypertrophic scars or keloids. Thus we are led to the conclusion that these conditions are not associated with any hereditary or nevoid tendency toward scar formation.

In various forms of fibroses we have found certain clinical and histologic differences. Clinically, some of the conditions involve the cutis

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38. Weiss, P.: Erzwingung elementarer Strukturverschiedenheiten am in vitro wachsenden Gewebe, Arch. f. Entwcklngsmechn. d. Organ. **116**:438-554, 1929.

39. Cowdry, E. V.: Textbook of Histology, ed. 2, Philadelphia, Lea & Febiger, 1938, p. 437.

40. Jordan, H. E.: A Textbook of Histology, ed. 8, New York, D. Appleton-Century Company, Inc., 1940, pp. 47-53.

41. Clark, W. E. Le G.: The Tissues of the Body, London, Oxford University Press, 1939, p. 38.

42. Aykroyd, O. E., and Zuckerman, S.: Factors in Sexual Skin Edema, J. Physiol. **94**:13-25, 1938.

itself, such as knuckle pads, scleroderma, acrodermatitis chronica atrophicans and nodular subepidermal fibrosis. Others are found below the cutis, and the skin is, as a rule, freely movable over them, for example, juxta-articular nodes and rheumatic nodules; some involve both the cutis and the subcutis, as juxta-articular nodes of long duration, tuberculosis nodules and leprosy nodules. Histologically, the differences are also those of location, as previously mentioned. In addition, juxta-articular nodes show three zones of tissue changes and vascular changes characteristic of syphilitic nodes. The rheumatic nodes show central liquefaction and palisade arrangement of fibroblasts around this central cavity. The acrodermatitis nodules show the loss of elastic tissue and intense atrophy of the epidermis. Scleroderma nodules are characterized by the excessive enlargement of the individual fibrous cells and their fasciculi. Nodular subepidermal fibroses consist of irregular stellate masses of fibrous tissue, and knuckle pads are essentially areas of increased density of the connective tissue of the deep part of the cutis.

SUMMARY AND CONCLUSIONS

Fibrous nodules of various kinds have been described.

Their clinical and histologic appearance varies.

Etiologically, slight oft repeated trauma is a large factor.

In the other instances the stagnation of the tissue fluids in disease is the probable cause.

No tendency to the formation of hypertrophic scars or keloids was found in any of the conditions described.

ELECTROSURGICAL REMOVAL OF PLANTAR WARTS

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AND
SAMUEL B. FRANK, M.D.
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This article is written to call attention to a method of removing plantar verrucae. The technic is not complicated and requires equipment which is found in most dermatologic offices and clinics. It does not incapacitate or cause postoperative discomfort to the patient. Little or no scar tissue results when proper technic is employed.

One of us (F.L.K.), while working with Giraudeau in the Hôpital Saint Louis in 1929, had the opportunity to use this procedure on many patients and found it a method of choice. Search of the literature on this subject reveals only a short note in a paper by Giraudeau,[1] who stated that with this technic it is possible to remove the reproductive papillae and hence completely eradicate the wart.

Standard textbooks recommend a vast number of methods, ranging from psychotherapy [2] to internal medication [3] through a gamut of physical agents,[4] ending with application of massive doses of roentgen radiation [5] and removal in the ordinary surgical manner with a scalpel.

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Dr. George Miller MacKee, Director.

1. Giraudeau, R.: Le bistouri diathermique. Technique et indications dermatologiques, Arch. dermat.-syph. Clin. Hôp. Saint Louis **2**:236-245 (June) 1930.

2. (*a*) Bloch, B.: Ueber die Heilung der Warzen durch Suggestion, Klin. Wchnschr. **6**:2271 (Nov. 26); 2320 (Dec. 3) 1927. (*b*) Scholtz, W.: Heilung der Warzen durch Suggestion, ibid. **7**:265 (Feb. 5) 1928. (*c*) Karrenberg: Heilung der Warzen durch Suggestion, ibid. **7**:601 (March 25) 1928. (*d*) Memmescheimer, A. M., and Eisenlohr, E.: Untersuchungen über die suggestive Behandlung der Warzen, Dermat. Ztschr. **62**:63-68 (Sept.) 1931. (*e*) Sulzberger, M. B., and Wolf, J.: The Treatment of Warts by Suggestion, M. Rec. **140**:552 (Nov. 21) 1934.

3. (*a*) Sutton, R. L.: Sulpharsphenamine in the Treatment of Warts, J. A. M. A. **87**:1127 (Oct. 2) 1926. (*b*) Lurie, S. A.: Verrucae Vulgares (Palmar and Plantar): Treatment by Intramuscular Injections of Bismuth Salicylate, Arch. Dermat. & Syph. **26**:95 (July) 1932. (*c*) Goodman, J., Jr., and Greenwood, A. M.: Verrucae: A Review, ibid. **30**:659 (Nov.) 1934.

4. Lewis, G. M.: Verruca Plantaris: A Method of Removal by Electrosurgery, New York State J. Med. **35**:869 (Sept. 1) 1935.

5. (*a*) MacKee, G. M.: Verruca Plantaris, in X-Rays and Radium in the Treatment of Diseases of the Skin, Philadelphia, Lea & Febiger, 1938, p. 276.

(Footnote continued on next page)

Suggestion therapy is reported to have proved effective in some cases. When it is successful no trace of the lesion is left. Any other method, therefore, should approach as closely as possible this ideal. Methods which use caustics and acids or curettage followed by desiccation are certainly far from it.

Another consideration that should be kept in mind is the factor of postoperative discomfort and incapacity experienced by the patient. With most of the aforementioned methods the result is a painful open wound that heals by granulation tissue filling the base.

We are aware of the roentgen ray method employed by Montgomery and Montgomery,[6] which, they stated, results in no pain or sequelae and offers 90.35 per cent cures, in comparison with about 70 per cent produced by conventional roentgen ray therapy. However, the Montgomery technic requires several treatments and a meticulousness of detail that might set pitfalls for physicians less experienced with this technic.

In recapitulation, it can be stated that the method of choice should be relatively simple, should produce little or no after-pain, should not incapacitate the patient and should leave little or no scar tissue to serve later as a source of pain to the patient and no sequelae, such as may occur after excessive doses of radium or roentgen rays.

It is our contention that the method herein described will adequately remove plantar warts with a minimum of pain and no appreciable scarring.

TECHNIC

Plantar warts only have been treated. No discrimination was made in the selection of patients to be treated as to whether they had solitary or multiple lesions. No patients with "mosaic warts," as described by the Montgomerys, were seen.

The patient lies face downward on a wooden table, and the foot, extending over the end, is elevated by a block or sandbag. The foot is cleansed thoroughly with soap and water. The area is then painted with 7.5 per cent tincture of iodine followed by 95 per cent alcohol. Anesthesia of the area to be treated is obtained with a 2 per cent solution of procaine hydrochloride containing a 1:50,000 dilution of epinephrine hydrochloride, which is infiltrated deeply under and surrounding the area of the wart.

A swab of sterile gauze saturated with a solution of hydrogen peroxide or of boric acid is applied to the affected area for two minutes. The

(*b*) Popp, W. C., and Olds, J. W.: Roentgen Treatment of Plantar Warts, Radiology **31**:218 (Aug.) 1938. (*c*) Belot, J.; Nahan, L., and Fichgrun: Le traitement des verruces plantaires par application unique de radiothérapie à haute dose, Bull. et mém. Soc. d'électro-radiol. méd. de France **27**:128-135 (March) 1939.

6. Montgomery, A. H., and Montgomery, R. M.: Roentgen-Ray Therapy of Plantar Warts, New York State J. Med. **41**:371 (Feb. 15) 1941.

purpose of this procedure is to remove the remaining alcohol, to soften the area and to afford a wet operating field to prevent surface sparking.

The cutting current from a spark gap, high frequency apparatus is employed. A foot switch is used but is not indispensable, as the current is turned on before the loop electrode is applied to the skin.

The indifferent electrode of ordinary diathermy metal approximately 12 inches (30 cm.) square is placed under the fully clothed patient. Contact against the skin is not necessary, but care should be taken that there is no metal between this electrode and the skin.

The active electrode is made by twisting a stock 8 mm. steel wire loop so that the remaining loop is 2 mm. in diameter. This twisted stem with the loop gives the electrode an overall length of 1 cm. (fig. 1).

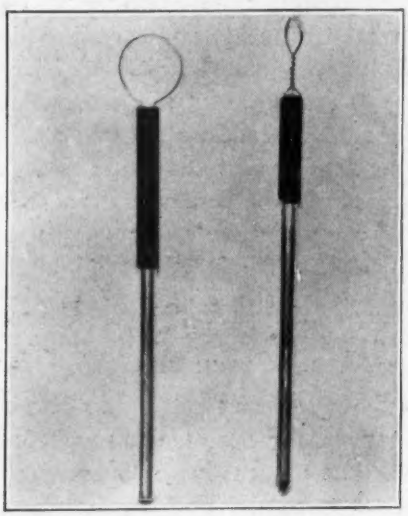

Fig. 1.—Twisted electrode loop.

By previous experiments with meat or soap one must determine the correct adjustments of the apparatus. The desired intensity is one that will allow the loop to penetrate easily while not producing excessive coagulation.

The electrode should be washed with soap and water and sterilized in 95 per cent alcohol before use.

The loop holder is held perpendicular to the surface of the wart, and with the current on, the loop is thrust into the center of the wart to a depth of 6 to 10 mm., depending on the size of the wart to be treated. With a continuous motion the loop is rotated 180 degrees on its own axis (a half-turn) and then is withdrawn from the same linear opening that was made when the loop was embedded in the tissue. By this rotating movement the essential part of the wart is destroyed.

Owing to a slight coagulation of the blood vessels, no bleeding occurs and after the electrode is removed only a linear incision the width of the loop is observed on the surface.

The wound is again painted with tincture of iodine, followed by alcohol, and a dry dressing is applied. The patient is advised to keep

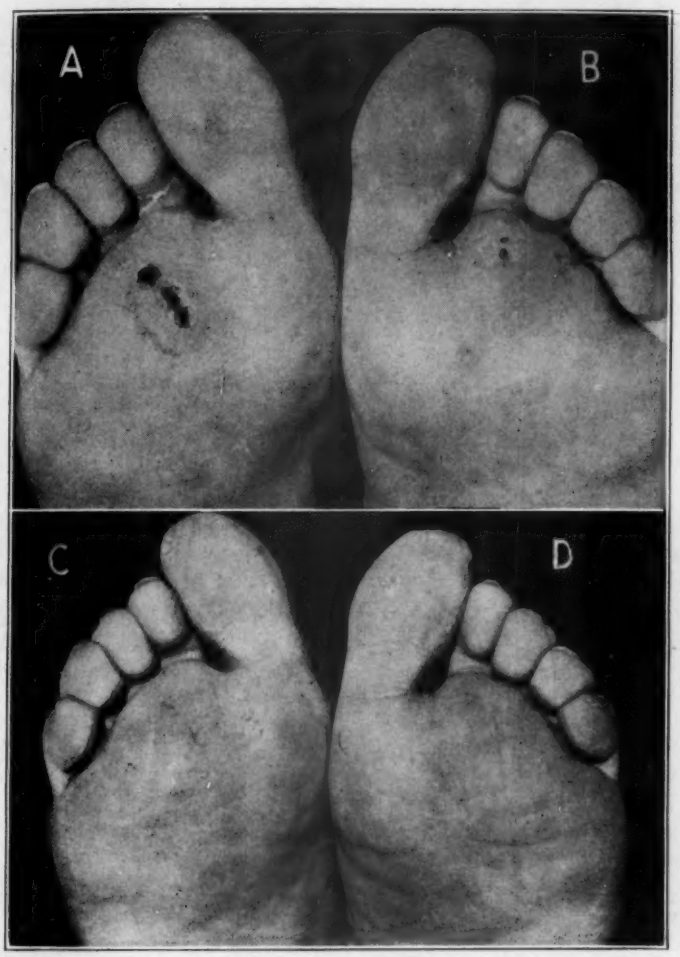

Fig. 2.—*A*, right foot one week after three warts were destroyed. *B*, left foot three weeks after five warts were destroyed. *C*, right foot five weeks after operation. *D*, left foot seven weeks after operation.

the foot dry for two weeks. Dressings are changed on alternate days. At the end of two weeks the patient is instructed to soak the foot in warm water for twenty minutes immediately before coming to the physician's office. The physician then removes the superficial crust. This

practically finishes the treatment. A total of three or four weeks is required for complete healing and disappearance of all evidence of treatment and of the wart. The patient can continue his vocation from the beginning of treatment without discomfort. In fact, most patients are more comfortable after than before treatment.

OBSERVATIONS

Twenty-one patients with single or multiple warts on one or both feet have been treated and followed for over a year in the clinic. There were in all sixty lesions. Two of these patients with three lesions did not obtain relief with this technic. One of them had been previously treated by other means to which he also did not respond. All of the other fifty-seven lesions were completely obliterated.

REPORT OF A CASE

S. S., a girl aged 18, in April 1940 presented a plantar wart on the right heel of seven to eight months' duration. She complained of severe pain in walking and limped considerably. Various pads and home remedies had been used without relief.

The lesion measured 4 by 5 mm. and was slightly raised above the surface of the skin. The surface was rough, and an areola of callus about 3 cm. in diameter was present. The slightest manual pressure seemed to produce excruciating pain.

The lesion was treated with the method described. The patient was seen two days after the operative procedure. She volunteered the information that the pain had completely vanished. After the anesthetic effect had worn off, she had only the slightest discomfort, which did not in any way incapacitate her. On the second day, pain had entirely disappeared, and only a feeling of fulness was noted about the area. This sensation persisted for about a week and finally disappeared. Examination on the second day revealed a linear crust approximately 3 mm. in diameter and no other changes. At the end of two weeks the treated area contained several ecchymotic points. The tissue appeared darker than normal and friable. This tissue was curetted gently with a dull instrument, and the crust was pared away. A small circular cavity resulted which was clean and did not bleed.

Examination two weeks after this revealed complete healing with the skin smooth and soft. A small ecchymotic area, no more than 1 to 2 mm. deep in the tissue, was noted at the site of the wart.

The patient was recalled eleven months later and was unable to identify on which foot the wart had been. Careful examination of the site showed the area to be smooth, and only with the aid of a lens was a minute (1 mm.) bluish point noted in the depth of the skin.

COMMENT

The average plantar wart if present for more than one or two months must be regarded as a deep lesion. It has been our observation, as well as that of most other physicians, that a fully developed wart usually has a depth of from 6 to 10 mm. below the surface of the skin. Consequently, any method of therapy that is too superficial is likely to fail.

The loop herein described satisfied this essential, and by using it properly it is possible to extend to the bottom of the wart.

The destructive effect of the cutting current used is limited only to the wart tissue and probably to the small capillaries nourishing the wart and to the adjacent nerve endings. Although there is no reason to believe that the cutting current as used here destroys every cell in the wart tissue, there is apparently enough destruction to tend to cause the remaining noninjured cells to die, owing to injury to sources of nutrition or other factors that are yet unexplained. Whatever the explanation, it has been observed in each instance that the treated area goes through a definite course of events as described, ending in the disappearance of the wart. The rapid subsiding of the pain seems to imply the destruction of the adjacent nerve endings.

SUMMARY

A technic for the destruction of plantar warts by means of the electrical cutting current is described.

This method has been used for the past eleven years by one of us (F. L. K.) with complete satisfaction and for over a year at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

Results with this procedure are more nearly ideal than with any other form of treatment, since postoperative discomfort and formation of scar tissue are reduced to the minimum and the technic is simple.

The percentage of cures in the 21 reported cases is 90.48.

This method is recommended for the routine treatment of plantar warts.

20 West Eighty-Fourth Street.

580 Fifth Avenue.

XCVII. ERYTHEMA ELEVATUM DIUTINUM

REPORT OF A CASE WITH HISTOLOGIC AND BACTERIOLOGIC STUDIES

MARTIN F. ENGMAN JR., M.D.
ST. LOUIS
RICHARD O. PFAFF, M.D.
SAN JOSE, CALIF.
AND
ZOLA K. COOPER, PH.D.
ST. LOUIS

Bury [1] in 1889 described a small number of cases of a curious erythema of the hands in which there were nodular thickening and induration of the skin. This disease may have been the same condition described later by Crocker and Williams (1894) [2] and named by them erythema elevatum diutinum. In 1929 Weidman and Besancon,[3] in presenting 2 cases, made a comprehensive bacteriologic and histologic study of the condition. From a lesion in one of the cases they isolated Streptococcus ignavus, which they suggested may have been a possible etiologic agent. They stressed in particular the rheumatic background in the majority of cases reported. Coombs and Bluefarb [4] in 1940 reported a case which histologically and clinically was similar to those of Weidman and Besancon. No attempt was made to carry out cultural studies.

We are reporting a case which histologically and clinically conforms to those described by the last two authors.

Studies, observations and reports from the Department of Dermatology of the Barnard Free Skin and Cancer Hospital and the Department of Dermatology, Washington University School of Medicine, service of Dr. M. F. Engman Sr.

Dr. L. A. Julianelle, Department of Applied Bacteriology, Washington University School of Medicine, assisted and gave advice in the bacteriologic studies in the case to be reported.

1. Bury, J. S.: A Case of Erythema with Remarkable Nodular Thickening and Induration of Skin, Associated with Intermittent Albuminuria, Illust. M. News **3**:145, 1889.

2. Crocker, H. R., and Williams, C.: Erythema Elevatum Diutinum, Brit. J. Dermat. **6**:1 (Jan.) 1894.

3. Weidman, F. D., and Besancon, J. H.: Erythema Elevatum Diutinum, Arch. Dermat. & Syph. **20**:593 (Nov.) 1929.

4. Coombs, F. C., and Bluefarb, S. M.: Erythema Elevatum Diutinum, Arch. Dermat. & Syph. **42**:441 (Sept.) 1940.

REPORT OF CASE

A. L., aged 60, a telegraph operator, was admitted to the Barnard Free Skin and Cancer Hospital on May 7, 1940. His chief complaint was the formation of plaques in the skin and about the joints. The lesions had appeared four years previously on both ankles over the lateral malleolus. At that time "they looked like little red pimples." These lesions became more inflamed and larger. At times there was a watery discharge with subsequent crusting and a certain degree of partial healing. A few of the lesions apparently healed spontaneously and left pigmented scars. Two years ago lesions appeared over the olecranon, on the dorsal surfaces of the joints of both hands, except the ring finger of the left hand, and on the dorsal surfaces of the toes. At varying intervals lesions appeared on the knees, on the posterior surfaces of the lower extremities, on the inner sides of the ankles and on the lateral and medial surfaces of both wrists.

The patient's history disclosed gonorrhea at the age of 24 and typhoid fever at the age of 42. During the early part of 1940 he had a mild recurring rheumatic pain in the left side of the neck and shoulder, which disappeared after the extraction of an abscessed tooth. A test of the urine for sugar one year prior to admittance gave a positive reaction.

The dermatologic examination showed lesions of varying sizes (0.5 to 3 cm.) on the following sites: the dorsal surfaces of the joints of both hands, except the ring finger, the lateral side of both wrists, the extensor surface of each elbow, the anterior surfaces of the knees, the anterior and posterior surfaces of the lower extremities, the dorsum of the foot, all joints of all toes of both feet and both heels. The characteristic lesions were plaques, which were round to oblong and pale red with pale summits. They were sharply outlined and definitely infiltrated. Each lesion could be lifted up en masse from the skin. The early lesions were small, 3 to 5 mm. in diameter, and were located on the right posterior surfaces of both extremities. They were flat, bright red and well outlined but had the same characteristic feel.

The general physical examination showed slight generalized enlargement of the thyroid. The blood pressure was 160 systolic and 60 diastolic. The estimated hemoglobin content was 86 per cent; the red blood cell count was 4,990,000, and the white blood cell count was 4,750. The differential count showed polymorphonuclear leukocytes 50 per cent, eosinophilic leukocytes 6 per cent and lymphocytes 44 per cent. The urinalysis disclosed a specific gravity of 1.017, an acid reaction, no sugar or albumin and, on microscopic examination, normal sediment.

The report of the laboratory studies made in another hospital a year prior to admittance to the Barnard Free Skin and Cancer Hospital was as follows:

Blood suger determinations (in milligrams per hundred cubic centimeters) in May 1939:

May 16, 78
May 19, 105
May 23, 115
May 26, 38
May 30, 118

Results of sugar tolerance test (in milligrams per hundred cubic centimeters) on May 10, 1939:

Fasting (9:30 a. m.), 80
First specimen (10:00 a. m.), 162
Second specimen (11:00 a. m.), 192
Third specimen (12:00 noon), 140
Fourth specimen (1:00 p. m.), 93

The results of a dextrose tolerance test (determinations made on the urine) on May 10, 1939:

Fasting	0.0 per cent
First specimen	0.0 per cent
Second specimen	0.0 per cent
Third specimen	2.0 per cent
Fourth specimen	0.3 per cent

Nonprotein nitrogen amounted to 20 mg. per hundred cubic centimeters of blood. A Kahn reaction was negative. An electrocardiogram was normal. The basal metabolic rate was + 25 per cent.

A biopsy specimen was obtained from a lesion on the left wrist. The epidermis showed marked hyperkeratosis and a thickening of the granular layer. There was a moderate degree of acanthosis, but the few rete pegs present were short and stubby.

Fig. 1.—Lesions on the hands of a patient with erythema elevatum diutinum on Nov. 12, 1940.

There was a relatively dense infiltrate in the cutis, especially in the upper portion. The infiltrate was made up largely of lymphocytes and epithelioid cells. Only an occasional polymorphonuclear leukocyte was found. Scattered in the upper part of the cutis were numerous small deposits of basophilic granular material. Some of these particles had been engulfed by phagocytic cells of the infiltrate. This material stained blue with Turnbull's blue reaction for the demonstration of iron and perhaps represented the remnants of red blood cells which had undergone degeneration. The superficial blood vessels of the cutis were dilated and the endothelial lining of these vessels hyperplastic. The cutis was edematous, and in the region below the infiltrate some of the collagen fibers showed hyalinization.

The patient remained in the hospital for two weeks. No definite diagnosis was made.

He returned to the hospital on Nov. 12, 1940 (a lapse of six months), with no appreciable change of the lesions (figs. 1 and 2) except that a few had broken down and presented superficial ulcerations. A few new lesions had appeared on the posterior surface of the lower extremities. The results of a general physical examination were essentially the same as on the previous admittance. The blood count and the urine were normal. The fasting blood sugar amounted to 98 mg.

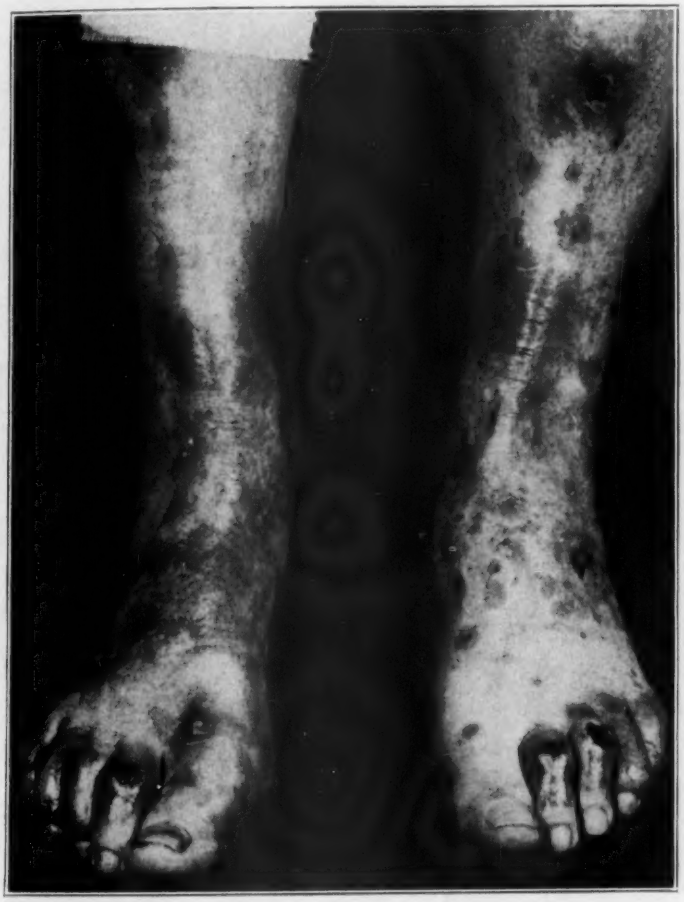

Fig. 2.—Lesions on the feet of the same patient as in figure 1.

per hundred cubic centimeters. A roentgenogram of the chest was normal. The basal metbaolic rate was + 9 per cent.

Another biopsy specimen was taken from a representative nonulcerated nodule on the right lower extremity. The epidermis showed relatively little pathologic change except for a moderate hyperkeratosis and a moderate degree of acanthosis. The rete pegs were short, somewhat thickened and in places fused (fig. 3).

In the cutis, however, there were edema of the collagen and dilatation of the lymph spaces. Throughout the corium, but especially about the blood vessels and

sweat gland ducts, a cellular infiltrate was conspicuous. The striking feature of this infiltrate was the presence of huge numbers of polymorphonuclear leukocytes (fig. 4). Epithelioid cells, fibroblasts and a few lymphocytes were also seen. This infiltrate was scattered between the collagen bundles throughout the entire

Fig. 3.—Low power photomicrograph, showing acanthosis of the epidermis, edema and dilatation of the lymph spaces of the corium and a cellular infiltrate throughout the corium.

thickness of the corium but was more dense in the upper third. All of the blood vessels were surrounded by a relatively thick collar of the infiltrate. The walls of the blood vessels were edematous with some evidence of hyalinization, and the lining endothelial cells were hyperplastic and their nuclei swollen (fig. 5). In

some instances the lumens of the vessels were almost obliterated, although there was no thrombosis. About the sweat glands and their ducts there were dense masses of polymorphonuclear leukocytes and epithelioid cells. The infiltrate extended even into the subcutaneous fat.

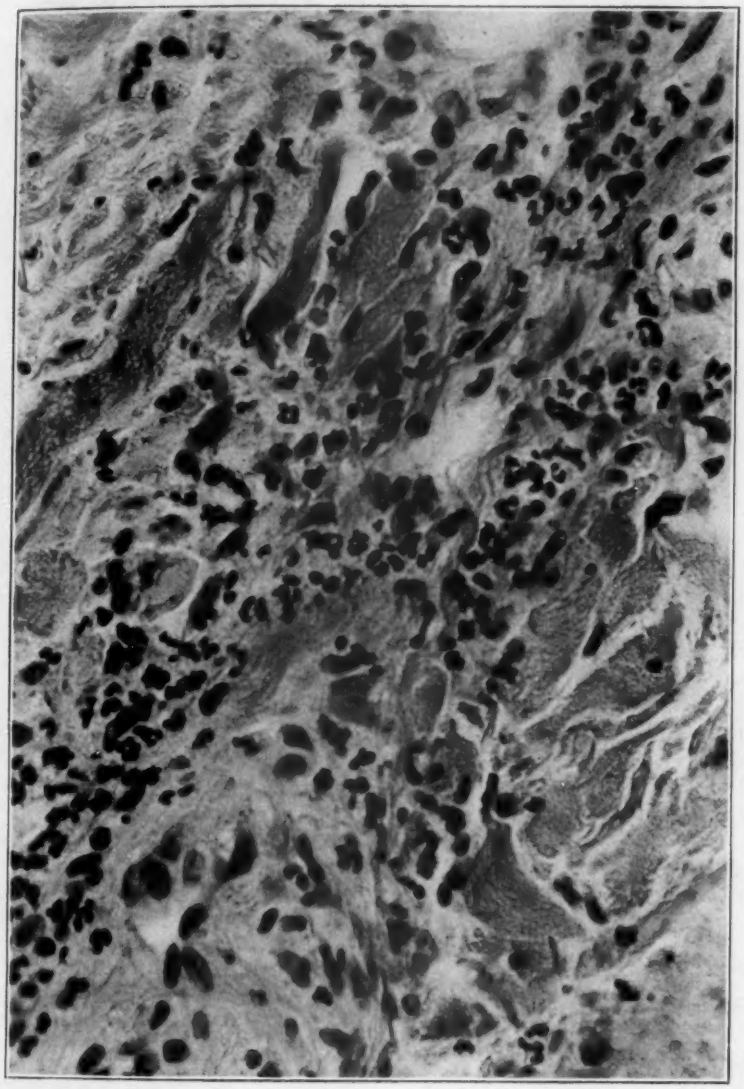

Fig. 4.—High power photomicrograph, showing the character of the infiltrate, which is made up predominantly of polymorphonuclear leukocytes with a few epithelioid cells and lymphocytes.

No bacteria could be found in the microscopic sections, and no areas of necrosis were demonstrable. As Weidman and Besancon [3] have pointed out, erythema elevatum diutinum is the only chronic "dermatosis (of the skin proper) in which

masses of polymorphonuclears dominate the picture." This type of infiltrate, together with the hyaline changes in the vessel walls, is pathognomonic of erythema elevatum diutinum.

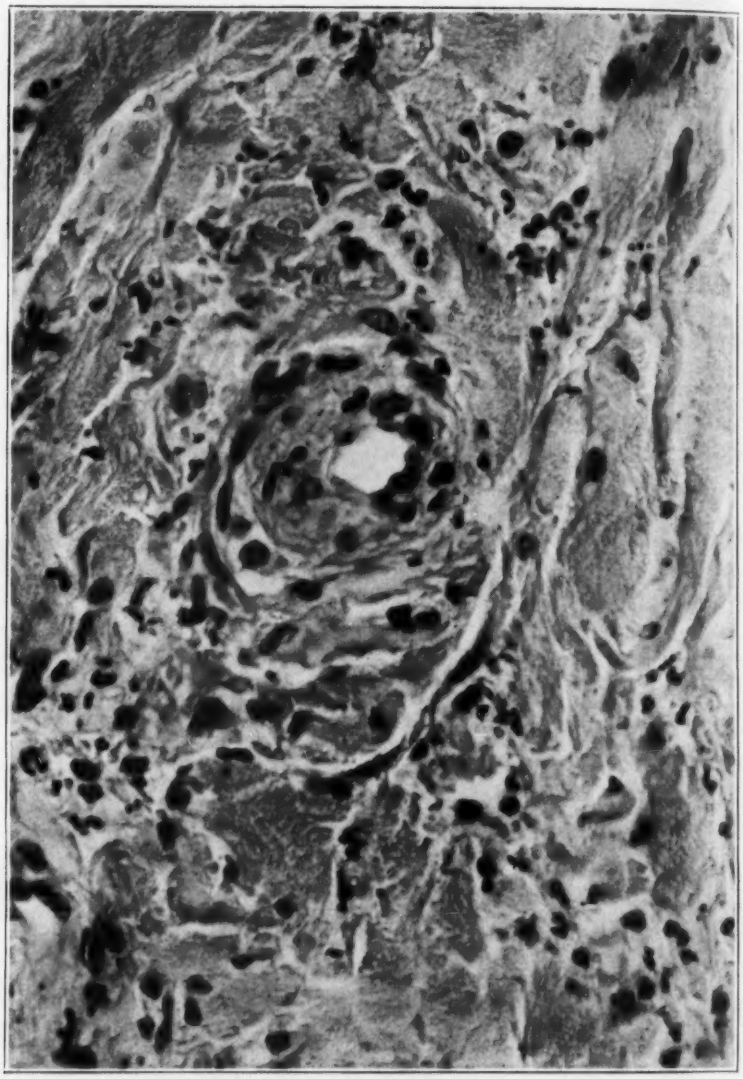

Fig. 5.—High power photomicrograph, showing a blood vessel surrounded by an infiltrate of polymorphonuclear leukocytes and epithelioid cells. The walls of the vessel are thickened and show evidence of hyaline degeneration.

An attempt was made to confirm the bacteriologic observations of Weidman and Besancon. A specimen was taken for biopsy under aseptic technic. The skin was thoroughly washed several times with tincture of green soap and water,

followed by alcohol. We felt that the surface was as free of contamination as possible. Sections prepared from the specimen were stained by the Gram method but revealed no bacteria. A culture was made from the ground skin. Preliminary smears showed no growth, and several cultures showed no growth after several days' incubation. A culture and smear were made from a swab which had been scooped into the subcutaneous tissue underlying the area from which the lesion had been excised. Both smear and culture showed no growth.

The patient was given sulfanilamide but was not able to tolerate the drug for more than four to five days at a time. He was then given a mild foreign protein by intramuscular injection every third day. The lesions began to regress, and many had disappeared when he left the hospital Dec. 23, 1940. Two months later the lesions on the legs had completely regressed, leaving deeply pigmented scars. Those on the knuckles of both hands were smaller but did not show complete involution.

SUMMARY

1. A case of erythema elevatum diutinum with histologic studies is reported.

2. A bacteriologic study failed to reveal any organisms.

SCLEREMA NEONATORUM

REPORT OF A CASE WITH AUTOPSY OBSERVATIONS

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BROOKLYN

Sclerema neonatorum is a rare disease occurring at or shortly after birth, characterized by a spreading induration of the skin and subcutaneous tissue from the lower extremities to the trunk, arms and face. The skin is reddish, purplish or mottled, cold, hard and leathery, while the subcutaneous fat becomes hard and rigid. It causes joints to be immobile, rendering impossible movements of the jaw, of the extremities and even of the thorax. Respirations become weak; the pulse is weak, and the temperature stays subnormal.

Babies suffering from sclerema neonatorum are usually small and undernourished and are often premature. They almost invariably die within a few days after the onset of the disease. Sclerema neonatorum is thus sharply differentiated clinically from the disease that has been called adiponecrosis subcutanea neonatorum or lipophagic granuloma. This condition is benign; it appears a few weeks after birth and invariably disappears spontaneously, usually after a few months. As a rule it leaves no permanent trace except slight atrophy in rare instances.

The cause of sclerema neonatorum is unknown, and as the disease is decidedly rare it seemed worth while to record the following case, especially as a complete autopsy was performed.

REPORT OF CASE

History.—A white male, full term infant was born spontaneously to a woman 42 years of age (a patient of Dr. J. Weinstein). The position was left occipitoanterior, and the pregnancy was not unusual in any respect. This was the patient's seventh pregnancy. She was in labor for three and a half hours, and after the delivery of the placenta by the Schultze method, a first degree laceration was repaired. There was no injury or instrumentation. Her measurements were ample, and she was otherwise normal on physical examination. Menstruation had begun at the age of 16, the periods lasting for four days and occurring irregularly every two to four months. Two infants were stillborn. The remaining children were living and well, the oldest being 23. There had been no miscarriages. The Wassermann reaction was negative, and the urine was normal. Her husband was in good health. There was no history of pathologic pregnancies or unusual diseases in the family.

Clinical Examination.—The infant weighed 4 pounds and 13 ounces (2,183 Gm.) and measured 17½ inches (75 cm.). He was noted to be fairly normal at birth

except that there was an unusual flaccidity of all the muscles, especially those of the neck. He took feedings with increasing difficulty and showed a slight decrease in weight, to 4 pounds and 11 ounces (2,126 Gm.), at death four days later. It was noted after two days that there was an abnormal infiltration of the subcutaneous fat tissue of the thighs and cheeks. A masklike countenance appeared, and the jaws became immobilized, making feeding extremely difficult. Feedings were spat up intermittently. The child was seen by a pediatrician a few hours before death and appeared stuporous.

All the extremities and the neck muscles were extremely relaxed, and there was a slight cyanosis of the hands and feet. The head was well formed; the anterior fontanel was soft and depressed, and the frontal prominences were prominent. The eyes were kept shut and could not be opened. The tongue was slightly coated. The heart sounds were regular but somewhat weak. Respirations were shallow, but the lungs were otherwise normal. The abdomen was distended. The skin over the external surface of the thighs, inguinal regions, cheeks and forearms exhibited definite uniform indurations which felt rubbery. The color was slightly icteric. The temperature ranged between 97 and 98 F. The clinical impression was sclerema neonatorum and icterus neonatorum. Despite the use of an incubator, dextrose clysis, oxygen and other stimulation, the infant died on the fourth day.

Postmortem Examination.—Gross Examination: The body was that of a male infant 4 days old, with moderate postmortem rigidity and marked lividity, weighing 4 pounds (1,814 Kg.) and with the following measurements: length, 43 cm.; occipitofrontal circumference, 34 cm.; suboccipitobregmatic measurement, 31 cm.; occipitomental diameter, 12.5 cm. and biparietal diameter, 8.5 cm. On the head, face, abdomen and back the skin was purplish, owing to postmortem lividity. It was moderately thickened and could be pinched into folds with difficulty. On the face the skin could not be lifted from the bony structures, and it felt leatherlike to the touch. There was an advance degree of enophthalmos, and the eyelids were separated with great difficulty. The eyelashes were sparse, and there were fine lanugo hairs on the entire posterior surface (legs, arms, neck and back). The fingers could be bent, and the other joints were mobile except for a slight limitation of motion about the shoulder joints, part of which was a postmortem effect. The hair on the cranium was blond. There were fine milia over the nose and nasolabial folds. Apparently most of the cutaneous rigidity was of the face, forehead and occiput, where the skin could be moved with great difficulty or not at all. The scrotum and penis appeared somewhat edematous. It is also of interest to note that a caput succedaneum was entirely absent. The veins on the head appeared somewhat prominent, and the entire network of veins was visible. The face was yellow and the expression masklike. The fontanels presented the usual separations. The umbilical stump was about 1 inch (2.5 cm.) long and almost completely mummified. On midsection the skin and fat presented no gross abnormalities. The edge of the liver was found to extend 2.5 cm. below the costal margin.

On removal of the breast plate, the left pulmonary space contained about 10 cc. of thin cloudy yellow serofibrinous exudate. There were numerous delicate fibrinous "violin string" adhesions between the parietal and visceral pleura, which were easily broken. The mediastinal surface of the left lung was covered by a thin coating of yellow fibrinopurulent material. The right lung was covered at the costophrenic edge of the lung by a similar fibrinopurulent exudate. The intestinal loops were matted together by the same type of exudate, and there was about

15 cc. of thin yellow serofibrinous exudate in the abdominal cavity. The colon was unusually large and wide, measuring 2 cm. in circumference. The serosal surface was greatly engorged, and the large colon appeared to be unusually long. The sigmoid portion of the colon formed a large "S" and extended again up to the transverse colon before entering the ampulla. The pericardial sac contained a similar fibrinopurulent exudate. The epicardium and the pericardium appeared to be greatly engorged.

Thymus: The thymus was "H" shaped and situated astride the aorta in its usual position. It appeared to be slightly diminished in size, measuring 1.5 by 2.5 cm.

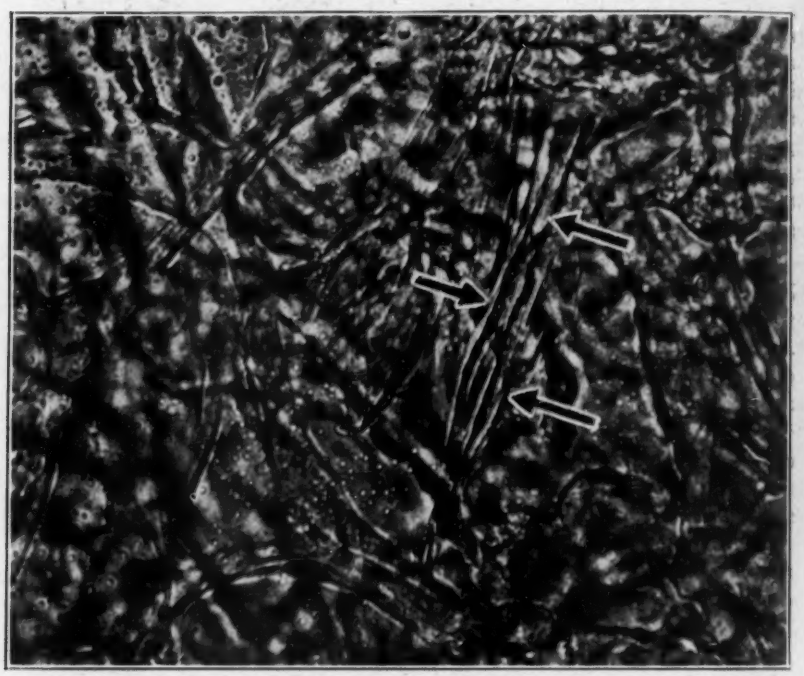

Fig. 1.—Section stained with sudan III, demonstrating a sheaf of acicular neutral fat crystals (× 800).

Heart: On section the heart appeared entirely normal except for a patent foramen ovale. No other congenital abnormalities were found. The endocardium and the valves were entirely normal. The aorta and the large blood vessels were of normal width and appearance.

Adrenals: The adrenal glands were normal in size and shape and presented no gross abnormality. The cortex and the medulla appeared to be grossly normal except for small hemorrhages.

Kidneys: The kidneys presented the usual number of fetal lobulations. The cortex and the medulla were sharply demarcated. The kidneys measured 3.5 by 2 cm. The papillae appeared as glistening white raylike structures owing to the presence of uric acid infarcts.

Ureters: The ureters were slightly tortuous and definitely widened, being about three times wider than normal and 0.9 cm. in circumference. As they approached the pelvis they became even wider. The bladder appeared to be normal, grossly, as did the prostate.

Spleen: The spleen was covered by a thin fibrinous exudate which could be scraped from the surface quite readily. It was of normal size, shape and position and measured 3.2 by 2 by 1.5 cm. On section, the structure appeared normal.

Lungs: The anterior half of the upper and middle lobes of the right lung were fused. The lungs floated in water. The serosal surface was previously

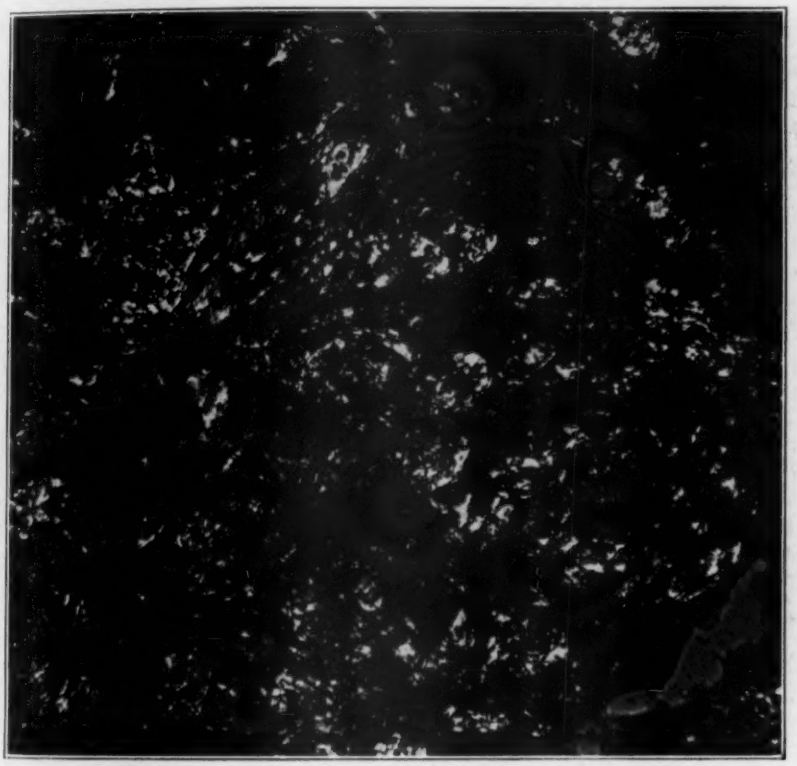

Fig. 2.—Photograph of sudan III stain (× 180) taken by polarized light with polarizers crossed. The crystals are seen to rotate the plane of polarization and shine up brightly throughout the section.

described. On section, the lungs presented no gross abnormalities. A thin serous fluid could be expressed from the cut surface. The left lung appeared somewhat duskier than the right and on section appeared slightly engorged, but no definite pneumonic consolidation could be found.

Liver: The liver was normal in position, shape and relations and measured 10 by 6 by 3 cm. On section the tissue appeared grossly normal.

Gallbladder: The gallbladder was embedded in the liver tissue and appeared to be rather long, measuring 3.2 cm. On section it was filled with a thick colorless mucoid material. There was no bile. The ducts were normal.

Gastrointestinal tract: The stomach appeared entirely normal, as did the esophagus. The intestines appeared to have undergone the normal transpositions. The colon was very long, as already described, measuring 42 cm. The appendix appeared to be normal, and the colon was filled with a thick, dark green meconium.

Pancreas: The pancreas was normal in size, shape and position and on section presented normal architecture.

Thyroid: The thyroid appeared to be small, sitting astride the trachea in the usual fashion.

Brain: The brain was opened in the usual manner. The sinuses were intact and the membranes normal. The cerebral vessels appeared somewhat engorged

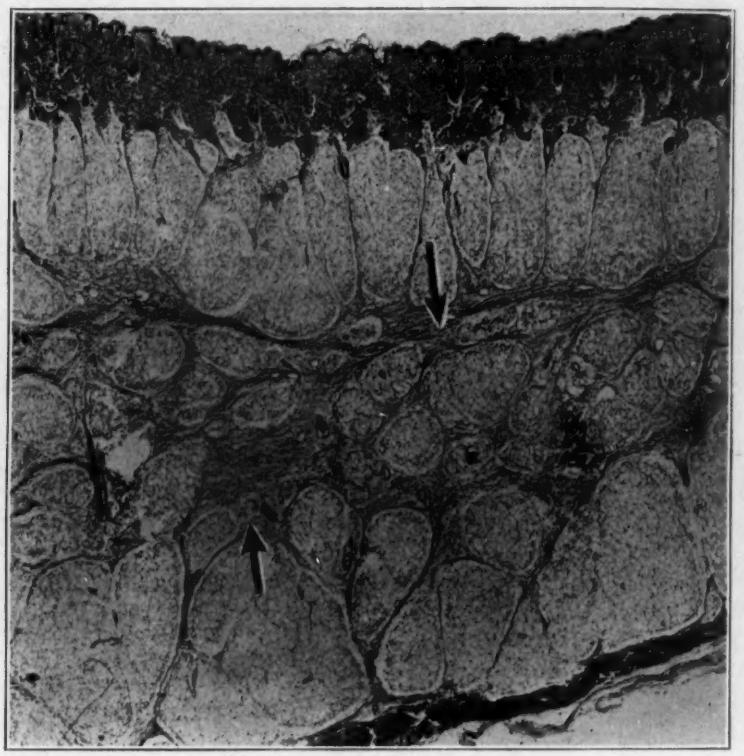

Fig. 3.—Section (× 11) through entire thickness of skin stained with hematoxylin and eosin, illustrating thickening and widening of the interlobular septums and cellular invasion of the lobules and septums.

externally. There was no hemorrhage. On serial section the brain appeared entirely normal.

Microscopic Examination: Skin: Examination of the cut surface revealed gross differentiation of the cutis from the underlying subcutaneous fat tissue, which had the appearance of a firm white lardaceous substance. Various stains were made of frozen sections as well as of paraffin-embedded sections. Two changes were apparent. First, there was noted the presence of colorless needle-like crystals lying in bundles or radiating tufts indiscriminately within the lobules

of the subcutaneous tissue (fig. 1). These acicular forms failed to stain with either sudan III or the osozone fraction of nile blue sulfate. However, on examination with polarized light these crystals of neutral fat were seen to rotate the plane of polarization (fig. 2). Secondly, there were seen a decided thickening and widening of the interlobular septums and disappearance of fat vacuoles along the periphery of the lobules with fatty changes. From the trabeculae masses of cells (foreign body giant cells, fibroblasts, lymphocytes and occasional leukocytes) invaded the fat lobules and septums (figs. 3 and 4). Proliferation of the foreign body giant cells was the reaction which occurred for removal of the crystals. The cutis and the epidermis were normal.

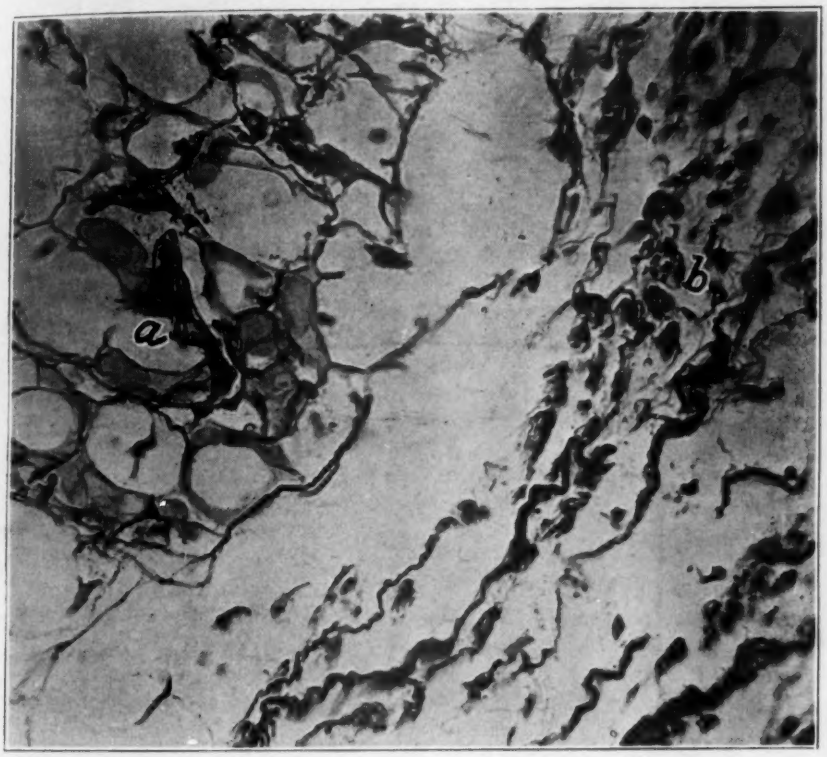

Fig. 4.—Section showing types of cellular invasion. A typical multinucleated foreign body giant cell is clearly visible at *a*, while the other cells (*b*) consist of fibroblasts, lymphocytes and a few leukocytes (× 400).

Lungs: The alveoli were dilated, and there were blood and blood pigment in the stroma. The blood vessels were dilated and engorged with red blood cells. The pleural surface was covered by a fibrinous exudate.

Liver: The sinusoids and blood vessels were engorged, and the stroma appeared normal.

Adrenals: Large areas of hemorrhage were seen throughout the adrenals.

Heart, kidneys, thymus and spleen: These organs exhibited engorgement of the blood vessels. In addition, the pericardium was covered by a fibrinous exudate

containing polymorphonuclear leukocytes. The kidneys presented uric acid crystals in the tubules.

Bacteriologic studies: Postmortem smears and cultures of the pleural and peritoneal fluid revealed a growth of Staphylococcus aureus.

Anatomic diagnosis: The condition was diagnosed as sclerema neonatorum; acute serofibrinous peritonitis, pleuritis and pericarditis; megalocolon; uric acid infarcts of the kidney; bilateral hydroureter; hemorrhage of the adrenals; patent foramen ovale; atrophic thymus; icterus neonatorum; inanition.

EXTENSIVE ALOPECIA AREATA OF DENTAL ORIGIN

EVIDENCE THAT ISOLATED AREAS OF ALOPECIA MAY BE DUE TO IPSILATERAL FOCI OF INFECTION

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As so little is known about the causation of alopecia areata, I am reporting a case in which the condition was apparently of dental origin.

REPORT OF A CASE

The patient, an American-born white man aged 29, was first seen by me on Dec. 22, 1936. At this time the scalp was entirely bald except for a preauricular vestige on each side. The eyebrows, eyelashes and beard were missing, as was all of the hair on the body except that of the pubic region.

The patient stated that he had first noted a gradual loss of hair of the scalp about three and one-half years previously, at which time the hair of both the scalp and the beard "commenced falling out in patches." He was seen by a dermatologist, who arranged for a complete physical examination and laboratory tests, the results of all of which were normal. At the onset of the disease he was employed in a drug store, but not being a pharmacist he handled no drugs and did not come in contact with mercury, arsenic, thallium or other heavy metals. Roentgenograms of the teeth which had been made at that time revealed an impacted lower third molar tooth and an apical infection in another molar tooth. The removal of these teeth was followed by a cessation of the alopecia and a regrowth of hair on the bald areas of the scalp in about six months.

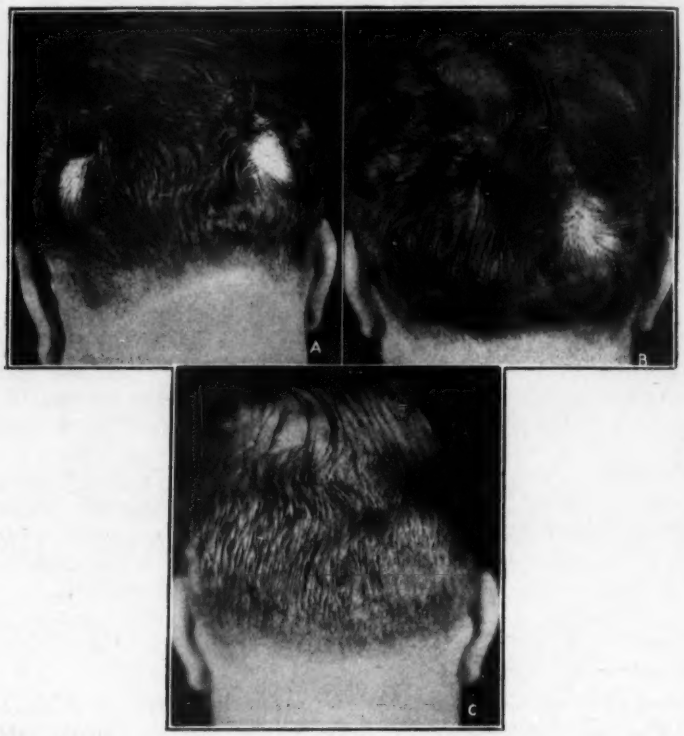
The patient's hair remained normal for approximately a year and a half, when it again began to fall, and within six months the loss of hair was as great as when he was first seen in my office.

When seen by me in December 1936 the patient had been hairless for approximately two years. He stated that he knew of no similar cases in his family. He did not recall any premonitory symptoms, such as burning or itching of the scalp, and had had no changes in the nails, such as white bands or brittleness. At no time had he observed adenopathy.

Complete dental roentgenograms revealed a dentition that was complete except for the four third molar teeth and the upper right second bicuspid tooth. The films showed no evidence of periapical infection, and the periodontal tissues were normal. The films, however, revealed one remarkable feature, that most of the posterior teeth held large silver amalgam fillings which to all appearances encroached on the pulp chamber, and that as far as could be determined they had not been properly protected by a base of cement to act as an insulator between the metal filling and the pulpal wall. It was my opinion that all of these fillings might have been embarrassing to the vital pulp tissue. Vitality tests of these teeth gave positive responses, and both objective and subjective symptoms were negative. The patient stated that almost all of the aforemen-

tioned dental repair work had been performed within three or four years prior to the onset of the alopecia.

In view of these facts it was decided to extract a few of the questionable teeth and to observe the results. Therefore, in December 1936 five of the teeth were extracted, four from the left side and one from the right. Within five to six weeks areas of lanugo hair were observed on the scalp. By the end of four months the growth of hair on the scalp was normal except for three or four coin-sized areas. The hair of the beard had also returned with the exception of scattered areas. At this time some parts of the eyebrows had regrown, but there



A, symmetric areas of alopecia. *B*, three months after extraction (Sept. 28, 1939) of second bicuspid on the lower left side. *C*, four months after extraction (Dec. 27, 1939) of second bicuspid on the lower right side.

was no indication of return of the eyelashes. In view of the persistence of these bald areas, in June 1937 the upper left second molar tooth was extracted. The patient was not seen again until March 1938, at which time two lower right molar teeth were removed. Within four months the growth of hair on the scalp was complete, the hair being of normal shade, texture and tensile strength. The hair of the beard was approximately normal except for a few small areas. At this time the eyebrows were still scant and a few eyelashes were present.

For a year and a half after these last extractions the patient remained asymptomatic, but in the summer of 1939 two symmetric areas of alopecia developed on the right and left sides of the occiput (fig. *A*). These areas were not atrophic. Investigation revealed the presence of rather deep fillings in the

lower left and lower right second bicuspid teeth (note that these are mate teeth). To ascertain whether these identical areas were ipsolateral manifestations of a right and a left focus, on September 28 the questionable tooth on the left side was extracted, and in three months the area on the left side had become covered with hair (fig. *B*). On December 27 the tooth on the right side was removed, and in four months the bald area on the right side showed a complete regrowth of hair (fig. *C*).

Cultures made from the last two extracted teeth showed no organisms. All the extracted teeth were split open, and in each case the dentinal tubuli between the floor of the cavity and the pulp chamber were found to be impregnated with silver, which had been absorbed from the filling material.

COMMENT

In 1858 Baerensprung [1] advanced the trophoneurotic theory, postulating that alopecia areata was due to disturbances of nutrition (and therefore function) of the hair papillae as a result of derangement of the trophic nerves serving them.

Sabouraud,[2] as well as Lailler, stated that the occipital region was the site of predilection in 50 per cent of their cases.

McCarthy [3] stated the belief that alopecia maligna occurs in about 4 per cent of the cases of alopecia areata and also that the eyebrows and lashes are peculiarly resistant to the disease process and that they fall out as a rule only in alopecia maligna.

Further evidence favoring Baerensprung's theory was brought forth in 1886, when Max Joseph [4] demonstrated that symmetric areas of alopecia developed on cats in seven to twenty-seven days when a bilateral removal of the spinal ganglion of the second cervical nerve was performed.

In 1932, however, Aubrun [5] performed a series of one hundred and seventeen operations similar to those reported by Joseph, operating on both the ganglion and the periphery of the second cervical nerve root in cats. Seventeen only of this series showed partial alopecia, and he concluded that no specific trophic action was demonstrable.

Grindon [6] emphasized the frequent observation of amalgam and gold fillings in the same mouth in patients with alopecia, as well as decayed teeth and other stomatic irritants.

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1. Baerensprung, cited by McCarthy,[3] p. 146.

2. Sabouraud, R., cited by McCarthy,[3] p. 154.

3. McCarthy, L.: Diseases of the Hair, St. Louis, C. V. Mosby Company, 1940, p. 155.

4. Joseph, M.: Experimentelle Untersuchungen über die Etiologie der Alopecia areata, Monatsh. f. prakt. Dermat. **5**:483, 1886.

5. Aubrun, E. A.: Pruritus and Hyperesthesia Caused by Partial Sensory Denervation: Experimental Alopecia—Contribution to Study of Alopecia Areata, Arch. Dermat. & Syph. **34**:564 (Oct.) 1936.

6. Grindon, J.: Alopecia Areata Neurotica, J. Missouri M. A. **15**:145 (May) 1918.

Jacquet [7] observed that alopecia areata is associated frequently with defective teeth.

The case herein reported has two features of interest: (1) the possible relation of dental filling material to the loss of hair and (2) epilation in a definite period of time of a right and a left area of alopecia, so symmetric that they may be termed "mirror images," following the extraction of right and left mate teeth.

I believe that this case supports the trophoneurotic theory of alopecia areata, especially when one considers the ipsilateral phenomena aforementioned.

Comparison of two views of the right occipital area in the illustration (*A* and *B*) shows a small growth of hair (*B*), and it is my belief that this is due to an overlapping of nerve fibers from the left to the right side.

SUMMARY

A case is presented of extensive alopecia areata of three years' duration. Complete recovery followed the extraction of several teeth, which were evidently not infected. As the pathogenesis of alopecia areata is unknown, I am reporting a case in which the gross causative factor apparently consisted of several teeth containing large fillings of silver amalgam. Negative cultures were obtained from the last two teeth which were extracted, but all extracted teeth showed evidence of absorption of filling material.

The case is reported for two reasons: first, to show that improperly filled teeth, though vital and asymptomatic, may possibly be the cause of alopecia areata; second, to give illustrations of ipsilateral cause and effect.

NOTE.—At the time of writing (April 1941) the patient's eyebrows and eyelashes are scanty, and none of the individual hairs are fully developed.

104 S. W. Trick Building.

7. Jacquet, L.: Nature et traitement de la pelade; la pelade d'origine dentaire, Ann. de dermat. et syph. **3**:97, 1902.

ERUPTION DUE TO SULFANILYLGUANIDINE (SULFAGUANIDINE)

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Among the relatively new derivatives of sulfanilamide to find a place in chemotherapy is sulfanilylguanidine [1] (now commonly called sulfaguanidine). The administration of this drug has been reported in the treatment of acute bacillary dysentery and as a preoperative and postoperative measure in surgical therapy of the colon. As in the case of other derivatives of sulfanilamide, the use of this drug has been observed closely for toxic reactions. From preliminary studies with this drug the toxic reactions are relatively less common and cutaneous reactions at present are especially rare. Marshall, Bratton, Edwards and Walker [1a] reported that no definite toxic effects were observed in their series of 25 children. Among 25 adults, toxic reactions occurred or were suspected in 3: fever and unilateral conjunctivitis on the second day in 1, possible mild hemolytic anemia on the third day in another and fever on the eighth day in another. Lyon [1b] seriously questioned whether any unfavorable symptoms observed among his 23 patients were traceable to sulfanilylguanidine and Firor and Jonas [1c] did not observe nausea or vomiting in their patients.

In the following case an eruption was associated with sulfanilylguanidine therapy.

REPORT OF A CASE

J. D., a 28 year old white man, was admitted to the medical service of the Cincinnati General Hospital with a history of chills, fever, abdominal cramps and profuse diarrhea, all of three days' duration. The history showed nothing abnormal except measles and scarlet fever as a child.

Physical examination revealed an acutely ill, confused, moderately restless patient with a temperature of 104 F., a pulse rate of 128 and a respiratory rate of 28. The skin was clear and dry. The tongue was heavily coated, and the

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From the Department of Dermatology and Syphilology, Cincinnati General Hospital.

1. (*a*) Marshall, E. K., Jr.; Bratton, A. C.; Edwards, L. B., and Walker, E.: Sulfanilylguanidine in Treatment of Acute Bacillary Dysentery in Children, Bull. Johns Hopkins Hosp. **68**:94 (Jan.) 1941. (*b*) Lyon, G. M.: Chemotherapy in Acute Bacillary Dysentery: II. Clinical Use of Sulfanilylguanidine, West Virginia M. Monthly **37**:54 (Feb.) 1941; Sulfanilylguanidine Treatment of Acute Bacillary Dysentery, U. S. Nav. M. Bull. **39**:279 (April) 1941. (*c*) Firor, W. M., and Jonas, A. F.: The Use of Sulfanilylguanidine in Surgical Patients, Ann. Surg. **114**:19 (July) 1941.

breath was foul. There was moderate injection of the pharynx. Transient rhonchi were noted in the chest. The abdomen was diffusely tender and moderately rigid. The liver and spleen were not palpable.

Examination of the blood showed: red cells, 4,760,000; white cells, 13,700; a differential count of 86 per cent neutrophils, 12 per cent lymphocytes and 2 per cent monocytes; urea nitrogen, 108 mg. per hundred cubic centimeters, and carbon dioxide–combining power, 31 cc. per hundred cubic centimeters. Examination of the urine showed a 1 plus reaction for albumin and rare white blood cells and granular casts per high power microscopic field. Cultures of the stool and urine and reactions to agglutination tests for the typhoid-dysentery group of organisms were negative.

On June 3, the day after admission, the patient began receiving sulfanilylguanidine, 15 grains (1 Gm.) every four hours. This treatment was continued until June 7, at which time the sulfanilylguanidine level in the blood was 7.8 mg. per hundred cubic centimeters. On June 10 a dusky red maculopapular eruption developed, scattered over the face, trunk and upper extremities. It was confluent on the face and forearms and somewhat urticarial on the flexor surfaces of the forearms, particularly at the wrists. A faintly pink macular eruption was present on the lower extremities. The eruption blanched on pressure, and no petechiae were noted. There were no lesions of the mucous membranes. The lymphatic glands were not enlarged. No manifestations were noted in the upper respiratory tract. During the four days previous to the onset of the eruption, the temperature had gradually risen from a normal range to 102 F. The day following the onset the temperature began to decline, finally reaching a level between 100 and 101 F. on the third day of the rash. It remained there for five days and then fell to normal. The blood sulfanilylguanidine level at the time the rash first was observed was 2.8 mg. per hundred cubic centimeters. The patient was taking no other drugs at this time. The day following its appearance the eruption progressed and became typically morbilliform. All superficial lymph chains were palpable. There was a blotchy enanthem on the soft palate. Examination of the blood revealed 12.7 Gm. of hemoglobin, a red cell count of 3,470,000, a white cell count of 12,500 and a differential count of 84 per cent neutrophils, 12 per cent lymphocytes, 2 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils. The blood sulfanilylguanidine level was 1.3 mg. per hundred cubic centimeters.

By June 12, two days after the onset, the rash was confluent and began to fade from the face. Two days later a generalized fine branny desquamation was noted. This persisted for about a week, at the end of which time the skin was entirely clear. The blood showed a trace of sulfanilylguanidine on June 12, which disappeared two days later. On June 14 the urea nitrogen content of the blood was 24 mg. per hundred cubic centimeters, and the Weil-Felix reaction was negative. The patient was discharged on June 24, the twenty-second hospital day, with a diagnosis of acute gastroenteritis and an eruption due to sulfanilylguanidine.

COMMENT

Sulfanilylguanidine is relatively less absorbed when given by mouth than are other derivatives of sulfanilamide, and consequently blood levels are comparatively low, being less than 5 mg. per hundred cubic centimeters. However, for these drugs in general there is no relation between the blood level and the appearance of cutaneous reaction. Perhaps the fact that sulfanilylguanidine is less readily absorbed is responsible

for the fact that it is relatively less toxic. In this case the drug was administered for five days, 15 grains every four hours, the total dose during the course amounting to 315 grains (20.5 Gm.). On the day administration of the drug was discontinued the sulfanilylguanidine content of the blood was 7.8 mg. per hundred cubic centimeters, while three days later, at the onset of the rash, it had fallen to 2.8 mg. Apparently the blood level of 7.8 mg. was slightly higher than that usually attained with the drug, but the difference was too small to warrant any comment.

SUMMARY

A generalized morbilliform eruption is reported in a patient who received sulfanilylguanidine (sulfaguanidine). The eruption appeared seven days after this therapy was started. The cutaneous reaction was associated with an elevation of the blood level of the drug to 7.8 mg. per hundred cubic centimeters, which is slightly greater than those levels which have been reported previously as within the therapeutic range of the drug.

This patient is reported with the permission of Dr. Marion A. Blankenhorn, Director of the Medical Service, Cincinnati General Hospital.

TESTOSTERONE PROPIONATE IN TREATMENT OF MALE POSTCLIMACTERIC DERMATOSES

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AND
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Definite clinical evidence is at hand that at various periods of the life cycle hormonal disturbances play undisputed roles in diseases of the skin. This is especially true of a hormonal gonadal disturbance, which is evidenced by such conditions as tinea tonsurans during childhood, acne juvenilis during adolescence, the so-called tumor of pregnancy of the alveolar processes, keratoderma climactericum of Haxthausen, senile vaginitis and keratosis senilis of the aged. Reichert [1] stated: "It is an old story that in juvenile acne, as in senile pruritus and in eczema of old persons, hormonal disturbances play a particular role and that a great many attempts have been made to influence these diseases with endocrine treatment."

It has been observed that inflammations of the skin in older men frequently behave according to a pattern all their own. It is not uncommon for even an uncomplicated and mild dermatitis to assume major proportions of an exfoliative dermatitis. In an older man, after the establishment of a dermatitis, the skin assumes an increasingly dry appearance and flakes off readily, as though the horny layer had lost the adhesive substances which bind it to the underlying layers. Intense itching, malaise, chills, loss of weight and strength and a slow response to remedial agents are noted among some of the characteristics, so that one is confronted with baffling problems in therapeusis.

It is with the supposition in mind that after the male climacteric there occurs a hormonal gonadal disturbance which acts as a complicating or influencing factor in these dermatoses that we tried the use of testosterone propionate as an aid in treatment.

Testosterone is an androgenic substance (a male sex hormone) derived from testicular tissue. Its chemical structure is known, and it is available in synthetic form. The synthetic compound testosterone pro-

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From the Pittsburgh Skin and Cancer Foundation.

1. Reichert, T.: The Treatment of Juvenile Acne, Pruritus Senilis and Senile Eczema with Testosterone Propionate (Perandren), Schweiz. med. Wchnschr. **69**:102 (Feb. 4) 1939.

pionate has been used by many investigators as an adjuvant in the treatment of various diseases of the skin.

Brünauer [2] used it successfully in the treatment of several male patients suffering from alopecia.

The first communication of the effects of androgen (androsterone benzoate) treatment in dermatoses occurring about and after the male climacteric appeared in the *Dermatologische Wochenschrift*.[3] Leipner reported the following cases:

Case 1.—A 67 year old man presented a senile dermatitis of the back and chest with intense itching, burning, easy fatigability, malaise and insomnia. These conditions responded favorably to ten injections of the androgen given daily. Leipner especially stressed the fact that the dryness, scaling and dull appearance of the skin were decidedly benefited.

Case 2.—A 71 year old man had a vesiculoerythematous eruption of the back, chest, forehead, ears, neck and eyelids of one year's duration. No improvement followed the use of roentgen rays and other antieczematous treatment. After eight injections of the androgen the skin and the general condition improved. Complete recovery occurred.

Case 3.—A 30 year old man suffered from eczema of the genitalia of two and one-half years' duration. The usual ointments and roentgen ray treatments had little beneficial effect. After eight daily injections of the androgen he became symptom free and remained so.

Case 4.—A 36 year old man suffered from recurrent eczema of the hands and arms for one year. The condition was so severe that he was unable to follow his occupation as a waiter. After eight daily injections of the androgen the cutaneous condition improved to such an extent that he was able to return to his occupation and remained symptom free.

Case 5.—A 27 year old man incurred a sulfur dermatitis a year previously as the result of treatment for scabies. His skin was dry and lusterless, and there were notable evidences of intense itching. Various ointments were used without any permanent benefit. After improvement there was always a relapse. Injections of an androgen were started, and after the sixth injection the itching disappeared completely and did not recur.

Molitch [4] used testosterone propionate in 22 cases of acne vulgaris without appreciable benefit.

Hamilton and Hubert [5] studied the effects of testosterone propionate on pigmentation. They based their experiments on the fact that hyperpigmentation or tanning is influenced by the endocrine system, as evi-

2. Brünauer, S. R., in Wise, F., and Sulzberger, M. B.: Yearbook of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1936, p. 415.

3. Leipner, S.: The Treatment of Cutaneous Diseases with Androgens, Dermat. Wchnschr. **103**:914 (July 4) 1936.

4. Molitch, M.: Treatment of Acne Vulgaris with Testosterone Propionate, Endocrinology **23**:803 (Dec.) 1938.

5. Hamilton, J. B., and Hubert, G.: Photographic Nature of Tanning of Human Skin as Shown by Studies of Male Hormone Therapy, Science **88**:481 (Nov. 18) 1938.

denced by the bronzing which occurs in Addison's disease and by the physiologic hyperpigmentation which occurs during pregnancy. Their clinical observations had to do with 3 surgically castrated and 4 hypongonadal men, in all but 2 of whom the skin was pasty, sallow and gray. After the use of androgenic substances, the skin of these patients became more oily and more tanned, and there seemed to be a more luxuriant growth of hair. Some of the increase in the pigmentation was apparently due to previous exposure to actinic rays. The authors reported the following case:

In one case an orchidectomy was performed in May 1937. After this operation the patient noticed that he sunburned easily without tanning. In August he spent each morning and afternoon on a beach clad only in a bathing suit. Only a slight tanning resulted from this exposure to the sun. During the following December and January the skin was decidedly sallow. In January 1938 injections of testosterone propionate were started, and within three weeks there appeared tanning of his face and of that portion of his body which had been exposed to the sun during the summer. When the administratiton of the androgen was stopped the hyperpigmentation disappeared and the patient's skin again became sallow. Resumption of the injections resulted in the reappearance of tanning.

The authors likened tanning to the process in photography in which a developer is needed to bring out the image on a photographic plate. They considered that hormones act as such a developing agent.

Reichert [1] used testosterone propionate in a variety of instances and gave the following case reports:

Case 1.—A 17½ year old student suffering from a severe acne of the face, back and chest showed decided improvement after twelve injections.

Case 2.—A 20 year old student who resisted all types of treatment for acne responded well after twelve injections.

Case 3.—A 60 year old man had generalized pruritus of the hands, forearms and legs of five years' duration, with the development of an atypical eczema in the last three years. The patient had been impotent for the last eight years. After the fifth injection of testosterone propionate the itching lessened, and after ten injections he was so much better that this medication was stopped. The eczema disappeared completely. Two months later, after an attack of influenza, there was a recurrence of itching. Four injections were sufficient to stop it.

Case 4.—A 40 year old traveler presented, in addition to generalized pruritus, symptoms of depression. He looked much older than his age. He suffered from intense itching in the last two years and complained of frequent headaches, insomnia, malaise, impotence and easy fatigability. His skin was dry and inelastic, especially on the neck and the extremities. After ten intramuscular injections of testosterone propionate, which were given during a period of three weeks, his general condition improved. After six more injections he gained weight, his skin became softer and normally moist, and the pruritus, nervous symptoms and impotence disappeared.

Thus, Reichert reported that through the use of testosterone propionate he succeeded in bringing about decided improvement in 2 cases

of acne, in 1 case of senile pruritus associated with senile eczema and in 1 case of pruritus associated with nervous depression.

Lafitte and Huret [6] used injections of testosterone acetate in 3 women with psoriasis and in 2 women with eczema. They reported excellent results.

Edwards, Hamilton and Duntley [7] used crystalline testosterone propionate successfully in 7 patients with organic vascular disease. They based the rationale of treatment on a previous study of the skin of human castrates, which they observed to be deficient in arterial blood (Edwards and Duntley showed this with the recording spectrophotometer [8]). Injections of testosterone propionate increased the blood volume in the deficient arterial areas.

Riley [9] used testosterone propionate in 20 cases of acne vulgaris and recorded slight but definite improvement.

Cornbleet and Barnes [10] treated 46 patients with acne vulgaris with testosterone propionate given intramuscularly. The results were promising.

Henschen [11] used testosterone propionate in treating a 74 year old man who complained of severe burning and itching of the soles and palms, of being tired and of having vertigo. The palms and the soles were greatly thickened, giving an appearance of turtle shell. He likened this senile keratosis of the hands and feet to keratoderma climactericum of Haxthausen. After eight injections of 5 mg. of testosterone propionate, the condition melted away as if by magic.

Most of the communications found in the literature thus show that androgen is a therapeutically active substance. In commenting on the nipple test of Jadassohn,[12] Wise and Sulzberger [13] stated, among other

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6. Lafitte, A., and Huret, G.: Therapeutic Action of Androgens in Certain Types of Psoriasis and Eczema, Presse méd. **47**:472 (March 29) 1939.

7. Edwards, E. A.; Hamilton, J. B., and Duntley, S. Q.: Testosterone Propionate as a Therapeutic Agent in Patients with Organic Disease of the Peripheral Vessels, New England J. Med. **220**:865 (May 25) 1939.

8. Edwards, E. A., and Duntley, S. Q.: The Pigments and Color of Living Human Skin, Am. J. Anat. **65**:1 (July) 1939.

9. Riley, I. D.: Testosterone Propionate in Acne Vulgaris, Brit. J. Dermat. **51**:119 (March) 1939.

10. Cornbleet, T., and Barnes, B.: Hormones and Acne Vulgaris: Urinary Assay for and Therapeutic Use of Androgen, Arch. Dermat. & Syph. **40**:249 (Aug.) 1939.

11. Henschen, C.: Keratoderma Senilis of the Hands and Feet and Its Treatment with Perandren, Schweiz. med. Wchnschr. **70**:690 (July 20) 1940.

12: Jadassohn, W.; Uelinger, E., and Margot, A.: Nipple Test: Studies in Local and Systemic Effects on Topical Application of Various Sex Hormones, J. Invest. Dermat. **1**:31 (Feb.) 1938.

13. Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1938, p. 472.

things, that testosterone propionate dissolved in a proper medium is absorbed through the skin and that the local effects of this substance on the cutaneous organs can be objectively demonstrated.

In the last eighteen months we have observed the therapeutic effect of the use of androgen in a group of dermatoses which occurred in men about and after the climacteric period. The results were so satisfactory that we believe a review of the case reports to be of value.

In this group of cases synthetic testosterone propionate was used in the form of an inunction. The preparation was rubbed in over unaffected surfaces of skin; one inunction was used, which contained 4 mg. of testosterone propionate. Occasionally an itchy area would be anointed with this preparation, usually followed by amelioration.

REPORT OF CASES

CASE 1.—W. J., a white American aged 71, unemployed, presented himself on Jan. 4, 1940 on account of a dry, scaly, erythematous eruption which involved the scalp, face, shoulders, arms and various portions of the body. This eruption first appeared seven years previously and persisted during the winter months. He complained of intense itching.

The patient discontinued the use of soap and water, and the affected areas were covered with paste of zinc oxide N. F. Daily inunctions of testosterone propionate brought about a decided improvement in six days and a complete disappearance of itching after four more daily inunctions. The treatments were reduced to two each week, and they were discontinued on May 10. The patient spent the most comfortable winter in the past seven years.

CASE 2.—W. W., a white American aged 48, a detective, presented himself on Feb. 6, 1940 on account of a generalized, scaling, erythematous eruption which had begun one month previously on the scrotum. He complained of extreme itching. A diagnosis of contact dermatitis aggravated by topical applications was made. He was put to bed in a room stripped of rugs, hangings and all materials considered to cause aggravation of the dermatitis. Intravenous injections of calcium gluconate were given daily, and calamine lotion was applied. One of the features of the inflammation was puffiness. This was somewhat relieved at the end of three weeks, but the intense itching and the acute inflammation of the skin persisted.

On February 27 daily inunctions of testosterone propionate were begun. A decided improvement was noted at the end of a week, and the patient recovered completely and resumed his occupation on April 1, 1940.

Later he was given patch tests with various contactants. A strongly positive reaction was obtained from a patch test with material from yellow-dyed velour chair covering, which had been purchased one month previous to the onset of the attack of scrotal dermatitis.

CASE 3.—J. B. M., a white American aged 61, a produce merchant, presented himself on April 15, 1940 on account of a generalized eruption of three months' duration. This had begun on his buttocks and spread to his neck, face, arms, hands and legs. He complained of intense itching, anorexia, insomnia, chills and loss of strength and weight.

The patient was instructed to stay at home and to remove all his constricting clothing. Soap, water, tobacco and alcohol were interdicted. Daily injections of calcium gluconate were given. Paste of zinc oxide N. F. was applied, and 75 r of roentgen rays were given to carefully selected areas once each week for a month. At the end of this time there was little improvement.

On May 31 he was given daily inunctions of testosterone propionate. Improvement was noted in two weeks. On August 1 he was well, and his treatment was discontinued.

During the course of treatment it was determined that his dermatitis resulted from a pyogenic infection around the buttocks and spread as the result of harsh medication.

CASE 4.—C. B. L., a white American aged 62, a clothing salesman, presented himself on June 14, 1940 on account of a generalized, scaling and erythematous exfoliative dermatitis which had started two months previously. The eruption began on the nape of his neck, where a starched collar rubbed. Soon his entire body was involved. He complained of intense itching, chills and anorexia. There was a generalized enlargement of all the lymph nodes.

He was confined to his home; all constricting clothing was removed, and the use of tobacco and the taking of baths were stopped. He was given a bland diet. Daily intravenous injections of sodium thiosulfate were given. Paste of zinc oxide N. F. was applied, and a few carefully chosen, extremely itchy areas were treated with 75 r of roentgen rays. Two weeks later the patient's condition remained unimproved; so instead of the sodium thiosulfate calcium gluconate was given. No improvement was noted after two weeks.

On July 31 daily inunctions of testosterone propionate were started. In two weeks a decided improvement was apparent. Anorexia, chills and itching abated. The extreme erythroderma diminished, especially over the areas where the androgen ointment was applied. The administration of this ointment and of paste of zinc oxide N. F. was continued for four weeks. The inunctions were stopped on August 15 but had to be resumed one week later since there were signs of recurrence of the dermatitis. At the end of eight more weeks the patient was able to return to his occupation. He kept on with testosterone propionate inunctions twice each week for three months. They were then discontinued, and since then he has remained well.

CASE 5.—H. S., a white American aged 74, an upholsterer, presented himself on Dec. 9, 1940 on account of a scaly erythroderma of seven months' duration. This had begun on his legs and spread slowly to his arms, forearms, thighs and back. The eruption was extremely itchy, especially at night. He complained of anorexia, malaise, insomnia, loss of strength and loss of weight.

The patient was instructed to remain at home and to remove any constricting clothing. Soap, water, tobacco and alcohol were interdicted. As his legs were edematous, he was instructed to keep them elevated and to cut down on his fluid intake. At the end of two weeks no improvement was noted.

On December 27 the patient was given daily inunctions of testosterone propionate. Four weeks later his entire body was clear with the exception of the lower extremities. The inunctions were continued for another month. On Feb. 18, 1941, his entire skin was clear and the inunctions were discontinued. On March 11 a recurrence was noted, and the inunctions were resumed semiweekly. Since then the patient's skin and his general condition have been excellent.

CASE 6.—H. W. B., a white American, a shoe salesman, presented himself on Dec. 19, 1940 on account of a generalized erythematous scaling eruption. The

process affected his entire body except his face and scalp. It had begun six weeks previously and was attributed by the patient to an irritation occasioned by a suit of heavy underwear which he had worn without its first having been washed (this may have been a correct surmise, and the condition may have been a resin dermatitis). He complained of intense itching, anorexia, malaise, lassitude and chills.

He was confined to his home, and all constricting clothing was removed. The use of tobacco, soap and water was stopped, and he was given a bland diet. A few areas were treated with 75 r of roentgen rays. Paste of zinc oxide N. F. was applied, and calcium gluconate was injected intramuscularly daily. This treatment was continued for two weeks without improvement.

On Jan. 3, 1941 daily inunctions of testosterone propionate were begun. On February 4 the patient was decidedly improved. All his symptoms had either completely disappeared or were greatly ameliorated. The daily inunctions were discontinued. One week later the patient's condition was considerably worse and the inunctions of testosterone propionate were resumed. Improvement was noted almost at once, and cure was complete at the end of four weeks. There has been no recurrence since.

CASE 7.—H. G., a white American aged 66, a machinist, presented himself on Feb. 22, 1941 on account of an itchy and spreading dermatitis. The condition was of two years' duration and affected his hands and arms. Although he had been under the continuous care of several dermatologists, it had become progressively worse. Patch tests determined that a hand cream which he had used for a number of years caused a severe reaction. Discontinuance of use of the hand cream and institution of soothing treatment caused no amelioration of the dermatitis.

On March 22 he was given testosterone propionate inunctions, and within three weeks a great improvement occurred. The patient was well on May 24.

CASE 8.—W. F., a white American aged 59, an executive, presented himself on March 29, 1941 on account of a generalized dermatitis. He had been suffering from attacks of neurodermatitis about his elbows and one area on his buttocks for several years with an occasional flare-up. He also had a number of seborrheic warts on his back which occasionally caused severe itching. The last attack of neurodermatitis precipitated an acute and generalized dermatitis which affected his face, neck, shoulders, back, buttocks and legs and quickly became so disseminated that he had to be confined to his home. At the time of the first examination his skin was dry, harsh, red and extremely itchy. He suffered from chills, insomnia and general loss of strength.

The routine of restricting measures was applied, and paste of zinc oxide N. F. was used locally. This treatment made his condition decidedly worse. On April 18 inunctions of testosterone propionate were started. The eruption was under complete control on May 16. Since then semiweekly inunctions of testosterone propionate have been continued, as this has improved his general well-being.

SUMMARY AND CONCLUSIONS

Attention is called to the likelihood that hormonal disturbances play a definite role in the presenile and senile dermatoses of men. Symptoms of a generalized nature, malaise, chills and loss of weight and of strength accompany these eruptions.

Some of the literature describing the use of androgens for the treatment of dermatoses is reviewed.

The histories of 8 patients and the effects of inunctions of testosterone propionate are reported. The use of this substance in the treatment of presenile and senile dermatitis of men appears rational in view of the fact that cutaneous changes in the postclimacteric period appear to be a definite entity. In some instances this generalized dermatitis followed a definite local inflammation, such as (*a*) irritation produced by yellow-dyed velour chair covering, (*b*) pyoderma of the buttocks irritated by treatment, (*c*) irritation caused by rubbing of a starched collar, (*d*) resin dermatitis from cotton underwear and (*e*) a dermatitis caused by a hand cream.

In these patients amelioration of the symptoms began only after the use of inunctions of testosterone propionate. We believe that the use of this preparation in these presenile and senile dermatoses is of definite value.

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DERMATOLOGIC ASPECTS OF ROENTGEN RAY FIELD DISTRIBUTION

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An important but apparently neglected phase of roentgen ray therapy is the uniformity or, rather, nonuniformity of the field of radiation. It has been assumed by radiologists and dermatologists alike that the spatial distribution of the radiation is uniform and that the only nonuniformity of the field is due to the fact that the parts of the field remote from the center are farther away from the target than is the center. It has, of course, been known for many years that the distribution of radiation follows a modified cosine law, but the application of this knowledge in regard to the practical application of radiation seems to have been forgotten. On the simple reasoning of nonuniformity due to inverse-square law, it is easy to calculate the intensity at any point in the field. The results of such a calculation at a target-skin distance of 10 inches (25 cm.) are shown by curve 1 on chart 1 and curve 8 on chart 2. Actual measurements, however, vary enormously from the calculated values. Curves 1 to 7 and curve 9 on chart 2 show the results of these measurements on eight different types of commonly used apparatus. Thus, with a target-skin distance of 10 inches the calculated intensity at the periphery of a field 6 inches (15 cm.) in diameter would be 92 per cent of the center intensity. Measurements made on the eight machines gave a maximum of 96 per cent and a minimum of 20 per cent of the center field intensity. Obviously this condition will result in errors in dosage if it is not taken into account. This particular variation probably accounts for many of the unsatisfactory results in the three field treatment of facial acne and failures in the treatment of carcinomas at shorter distances.

Not only is there this variation from the calculated values at different distances from the center, but these variations are not symmetrically distributed about the center. Thus, for a given distance from the center the intensity is usually greater on the cathode end of the x-ray tube than

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it is on the anode end. For example, with a given machine at a target-skin distance of 8½ inches (22 cm.) the intensity 1 inch (2.5 cm.) off center on the cathode side was 110 per cent of the center intensity, while the intensity 1 inch off center on the anode side was only 75 per cent of the center intensity. At 2 inches (5 cm.) off center the intensities were 105 and 35 per cent respectively of the center intensity. This would mean that for large lesions one border would be getting more than the estimated dose, while the other border would be seriously under-treated. Chart 1 shows a typical distribution curve. It is seen that, although the drop in intensity is far greater than would be calculated, the

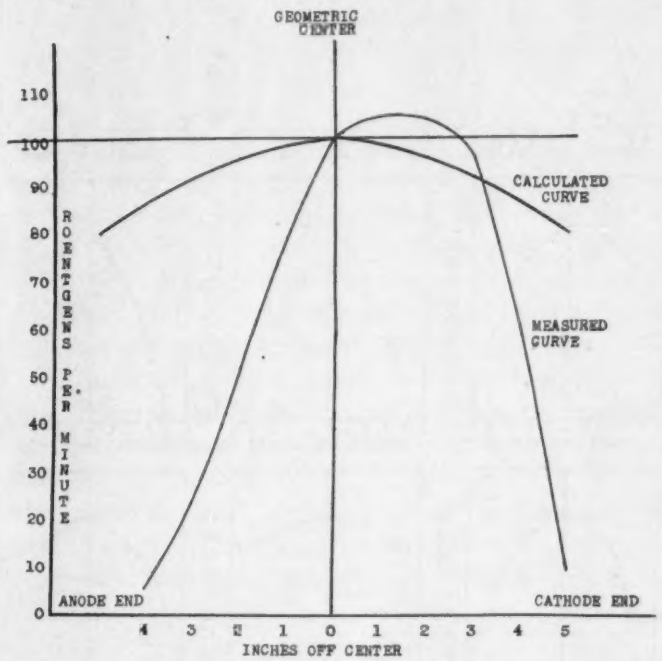

Chart 1.—Radiation distribution along the major axis of an x-ray tube. The measured curve shows that the radiation center is about 1¼ inch to the cathode end from the geometric center of the x-ray tube (target-skin distance, 10 inches).

curve is fairly symmetric with regard to the radiation along the major axis of the x-ray tube, provided *centering could be done 1¼ inches (3 cm.) to the cathode end of the true or geometric center of the x-ray tube.* It is readily apparent that centering must be accomplished with the utmost precision. This centering will be not necessarily at the actual center of the tube but should be at what may be termed the "radiation center," a point which must be determined by actual measurements of field distribution. Furthermore, this "radiation center" varies with the

target-skin distance used, which still further complicates the entire procedure. From chart 1 it is apparent that many manufacturers of dermatologic roentgen ray equipment have not given adequate attention to this factor.

The old style Universal type tube with its 45 degree anode did not exhibit as great a field distortion as do most of the newer shock-proof

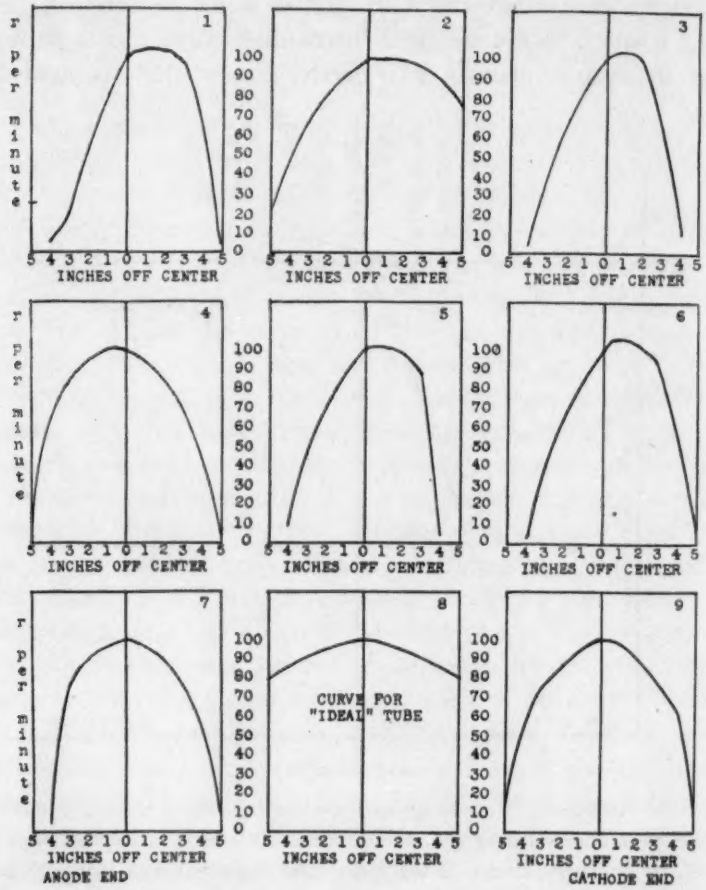

Chart 2.—Field distribution curves. These graphs show the roentgen ray field distribution of an ideal tube and that found on eight machines now popularly used by dermatologists (target-skin distance, 10 inches).

tubes, which have target angles considerably less than 45 degrees. However, even with these older tubes the use of the visible light reflected from the anode as a centering agent might well lead to errors in centering. Some of the newer equipment is provided with mechanical devices for centering. All equipment should be so provided, and dermatologists

having machines without such a device should obtain one, homemade if necessary. This device should, of course, indicate the "radiation center" rather than the geometric center of the x-ray tube.

Since measurements indicate this wide variation from calculated values in field distribution intensities, actual data must be obtained experimentally on all existing and all new apparatus. These data might well take the form of a straight line graph, which will indicate for the particular apparatus tested sizes of practically uniformly irradiated areas at various distances. One may arbitrarily, although with a degree of reasonableness, assume that a field which does not exceed 20 per cent variation at any point possesses "practical uniformity." The graph will then show sizes of fields having "practical uniformity" at various target-skin distances. This straight line graph should also show the 50 per cent boundaries, so that the proper "overlapping" technic for large areas may be evolved for the given machine. Chart 3 shows such a graph. It indicates, for example, that at a target-skin distance of 10 inches "practical uniformity" is obtained 1 inch from center on the anode side and 3½ inches (9 cm.) from center on the cathode side. In other words, with such a tube a practically uniform field 4½ inches (11 cm.) in diameter could be obtained, provided centering was done 1¼ inches to the cathode side of the geometric center of the x-ray tube. It also shows that 50 per cent of center intensity would be obtained 2 inches to the anode side and 4⅕ inches (10.5 cm.) to the cathode side. At a distance of 6 inches the graph shows that "practical uniformity" is obtained for a distance of ⅗ inches (1.5 cm.) on the anode end and 2 1/10 inches (5.5 cm.) on the cathode end. Chart 4 shows the results of tests on eight different machines.

Attention may be called at this point to the fact that this non-uniformity is a function of the design and construction of the x-ray tube and its housing and has nothing to do with the high voltage transformer or control or with the type of rectification—whether full wave, half wave or unrectified.[1]

The variation from machine to machine is evident. Curve 8, chart 4, shows "practical uniformity" for a tube in which the radiation would decrease according to the inverse-square law only. Analyzing this, one finds that for such a tube one could have a field of "practical uniformity" (not over 20 per cent variation) 10 inches in diameter at a distance of 10 inches or a field 20 inches (51 cm.) in diameter at a distance of 20 inches. If this is compared with the "practical uniformity" of any of the actually available tubes represented, they will be found to be far short of ideal.

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1. Ginsberg, J. E., and Landauer, R. S.: Unrectified Machines for Dermatologic Use: Clinical Considerations, Arch. Dermat. & Syph. **40**:53-58 (July) 1939.

Curves 4, 7 and 9, chart 4, show considerably more symmetry than any of the others. The reason for this is that the tubes used for these curves have approximately 45 degree anodes. The advantage of this angle is apparent. This does not mean that the 45 degree angle gives the calculated *amount* of radiation (compare these curves with curve 8, chart 2), but it does mean that the distribution of radiation along the

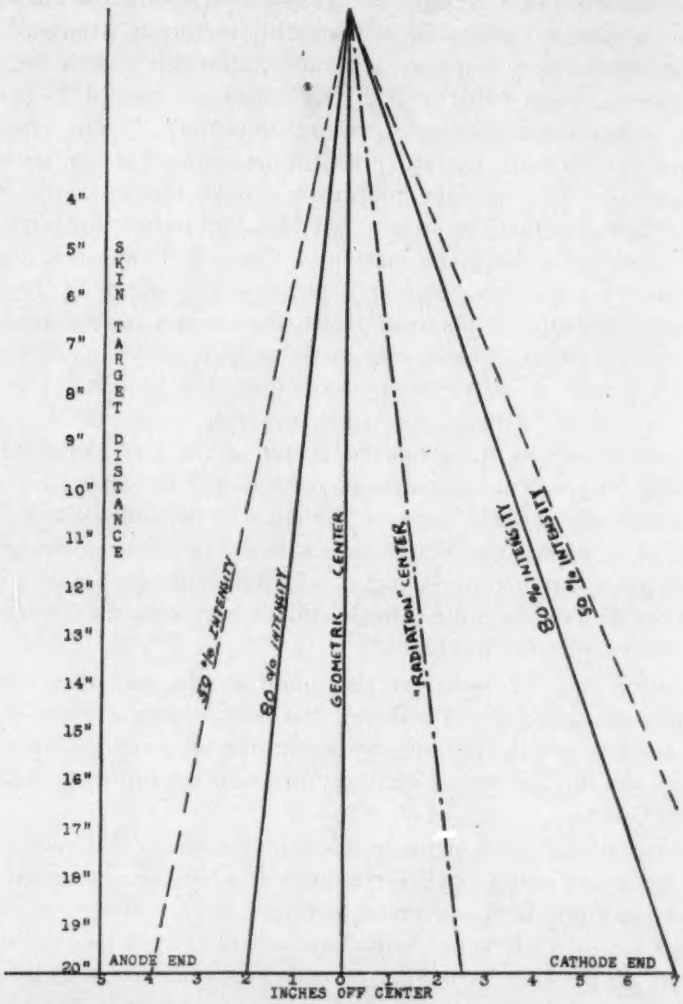

Chart 3.—Practical uniformity graph. All areas within the solid black lines received not less than 80 per cent of the intended dose. All areas within the dash lines received not less than 50 per cent of the intended dose. The dash-dot line represents the actual "radiation center" line.

major axis of the x-ray tube is more nearly symmetric with respect to the geometric center of the tube.

Obtaining reasonably uniform irradiation over multiple large fields, such as are used in treating extensive acne on the back, is impossible without one's first obtaining data on field distribution by actual measurement. Thus, with the "best" of the regular shock-proof tubes tested, "practical uniformity" is obtained with a 6¾ inch (17 cm.) field at a target-skin distance of 10 inches. With this same tube, 50 per cent edge intensity would be obtained with a field 9½ inches (24 cm.) in diameter. Hence, to get reasonable uniformity over a large area, the x-ray tube would have to be positioned every 9½ inches between centers. If this

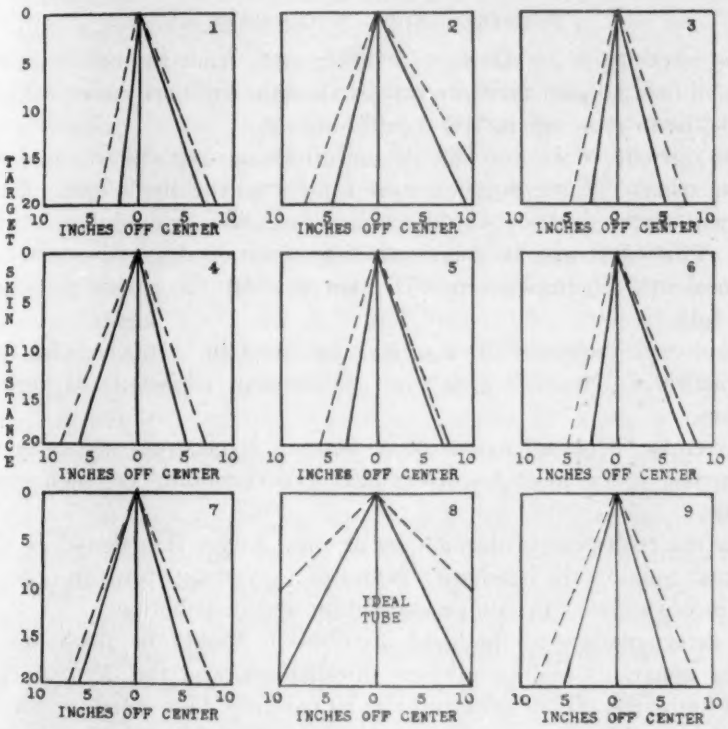

Chart 4.—Practical uniformity graphs and 50 per cent field edge intensities. The solid black lines show practical uniformity (not over 20 per cent variation). The dash lines show 50 per cent edge intensity.

value is compared with the calculated value of 18 inches (46 cm.) given by Andrews [2] and the values given by MacKee,[3] it is easy to see that considerable portions of the back would be definitely undertreated if too

2. Andrews, G. C.: Diseases of the Skin, ed. 2, Philadelphia, W. B. Saunders Company, 1938, p. 60.

3. MacKee, G. M.: X-rays and Radium in the Treatment of Diseases of the Skin, ed. 3, Philadelphia, Lea & Febiger, 1938, p. 388.

large intercenter distances were used. From chart 3 (which must be prepared from data on the given apparatus), the dermatologist, by observing the 50 per cent edge intensity, is able to estimate the exact intercenter distances for proper uniformity in dosage when using the overlapping technic for irradiation of large areas.

The lateral fields are not discussed in detail in this paper, although they were studied for the various types of apparatus tested. In general, they were found to show variations as might be expected, that is, between the extreme anode and cathode side variations.

SUMMARY AND CONCLUSIONS

The intensity of radiation at points remote from the center of the irradiated field falls off far more rapidly than the ordinarily used calculations of the inverse-square law would indicate.

The intensity does not fall off uniformly on opposite sides of the field but usually decreases much more rapidly on the anode end. X-ray tubes with approximately 45 degree anodes exhibit a minimum of this effect. This effect may be counteracted to a certain degree by centering at a measured "radiation center" rather than at the geometric center of the tube.

Graphs are suggested for use in determining the diameter of a field of "practical uniformity" (not over 20 per cent variation) at various distances.

Currently suggested modes of irradiating large areas are in error. The correct mode must be determined experimentally on each given machine.

For the treatment of dermatoses at short target-skin distances it is important to know the irradiation center of a given apparatus in order to avoid inconsistencies in dosage calculation and distribution.

A determination of the field distribution should be made on all existing apparatus and on all new installations, and the dermatologist should know the 80 per cent and the 50 per cent edge intensity for his particular machine.

JOB'S ILLNESS—PELLAGRA

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Substitution therapy for nutritional states is not new as far as the ancient Hebrews are concerned. It is a far cry from the manna of the wilderness to the nicotinic acid of the modern drug store counter. But illness due to the absence of nutritional factors in food was just as prevalent then as it is now. Wherever poverty has existed—whether it has been among the pyramid builders of ancient Egypt or among the share croppers of the Southern states, whether the toilers and peasants have subsisted on maize as their sole food or on cornbread, grits and syrup—in short, wherever an insufficient supply of nutritious food has existed and the diet has been lacking in the necessary vitamins, there has necessarily been a certain amount of deficiency disease.

Egypt was called the granary of the ancient world. Its lower classes subsisted chiefly on corn and grits. The vitamin B complex was unknown then, and nicotinic acid, the P-P factor effective in the prevention of human pellagra, was not included in the Egyptian pharmacopeia; yet diseases of the skin were common in those days. All the historians of antiquity wrote about "the Egyptian skin disease," and the Bible, in many of its pages, mentions "the evil diseases of Egypt," "the Egyptian Dermatitis" [1] and "the terrible incurable skin disease, *sh'chin raa,* that covers the knees and ankles, and involves the entire body from the soles of the feet to the crown of the head." [2] Such a disease attacked the patriarch-philosopher Job after he had lost his fortune and had become a pauper. "And Job was striken with a terrible skin disease, *sc'chin raa,* that involved his entire body from the soles of his feet to the crown of his head." [3]

The world did not need to wait twenty-two centuries for Gaspar Casal to open the story of pellagra in 1735, when he recorded his observations on "a malignant and most peculiar sort of leprosy" which was common among Asturian peasants whose chief source of food was maize, nor did it need to wait until 1771 for Frapolli [4] to recognize pellagra as a disease entity and for Marzari to postulate the theory that

1. Deuteronomy 28:27.
2. Deuteronomy 28:35.
3. Job 2:7.
4. Frapolli, F.: Animadversiones in morbum, vulgo palagram, Milan, J. Galeati, 1771.

it was not maize that caused the disease, but that maize in itself does not furnish sufficient amounts of certain essential nutritional elements.

When Goldberger in 1914 [5] opened the way for the eventual conquest of this dread disease, twenty-five centuries had witnessed a chaos and confusion during which suffering pellagrins were spat on as persons with syphilis, shunned as scabies-infested persons and locked up as lepers. If they who read the Bible had only understood what they were reading!

The Book of Job is a great philosophic treatise by one who was afflicted with pellagra, the nature of which was not recognized until two centuries ago. All Biblical scholars erred in diagnosing Job's grave illness. There can be no clearer description in the patient's own words than Job's complaints. No medical case history is more detailed. The prosaic physical torture and mental suffering which this disease gives rise to are depicted in poetic language throughout the forty chapters of this great book of the Old Testament.

Pellagra is a disease due to more than one deficiency factor and is characterized by a train of symptoms localized on the skin of the body with a general involvement of the various systems and organs. The first clear manifestation of the disease is the pellagral erythema, *sh'chin raa.* This is followed by desiccation and exfoliation of the epidermis, which becomes rough and dry, and occasionally crusts form, beneath which there is suppuration. With these cutaneous manifestations there are digestive disturbances which may be of a dysenteric nature. In the more severe and chronic forms there are pronounced nervous symptoms such as headache, spasms, backache, paralysis and mental disturbance, for instance, melancholia or suicidal mania. Finally, there may be severe emaciation and symmetric gangrene.

Job, in his misery and without relief of his symptoms, cried out: "O that my words were now written! O that they were inscribed in a book; that they were graven with an iron pen and lead in the rock forever!" [6] He appealed to scholars to study his physical plight and to find a remedy. He drew a perfect picture of this ailment. Twenty-five centuries later a modern Job drew a perfect picture of the same complaint that tortured the ancient Job. Dr. Baxter Haynes, of Spartanburg, S. C., who was a victim of this disease, reported [7] his own case before his medical society in Sumter, S. C., as follows:

> During the late summer and early fall of 1920, the great cotton slump and panic year came. When I realized the amount I had lost on cotton deals, I felt the keen dagger of financial reverses, I felt the sickening sting of something that had

5. Goldberger, J.: Pub. Health Rep. **29**:1683, 1914.

6. Job 19:23-24.

7. Haynes, B.: Internat. Clin. **4**:76, 1926.

vanished, something that most people worry about. Money! I felt a cog slip in that controlling part of my body, the dynamo, or nerve system and brain. I noticed my appetite beginning to fail; food became inedible and nauseating, and I suffered from insomnia to a marked degree. These were the first symptoms noticeable, which made me feel that I was not the same person that I had been for forty-one years.

These two disturbances, insomnia and anorexia, grew from bad to worse and . . . I'll say that I would go for a week at a time with no sleep at all, then a complete prostration would allow possibly twenty-four hours sleep.

The next noticeable symptoms were that my mouth, tongue and throat became very much irritated and finally this marked condition extended all the way from my lips to the rectum, involving all the gastro-intestinal tract. . . . This irritated condition of my mouth became so marked that my tongue became very red, thickened and stiff. My throat was so irritated finally it became difficult to swallow even water.

At just about this stage of this awful condition I became very melancholic, depressed and illusions were so marked that I wanted to live in exile. . . . I was obsessed with the idea that all my friends had forsaken me and that I was fighting the battle all alone. Of course, this was a figment of imagination, for no man ever had more friends than I, nor were any more beautiful services showered upon an unfortunate person.

At this stage I seemed to feel that it was a disgrace to have this condition, but I knew of no reason to feel that way about it, and even to this day, I know of no explainable reason. . . . Some of our local doctors who did not see me would make this remark: "Haynes does not have pellagra because he has always been a big eater, and has anything he wants." I had been a big eater and have always had an abundance of good things to eat, but very few people knew that for about eight or ten weeks I had quit eating, and they did not know that worrying was the cause.

Melancholia, mental depression and illusions became more marked and when my friends began to bring me flowers of every variety, baskets of fruits and many other delicacies. . . . I seemed to believe that such kind deeds of friendship had turned into a cold business or a routine act. . . . I know of no other painful condition in my former life or the present one where I ever felt the same way. Before going to the hospital I was very irritable with my family, and after doing or saying something uncharacteristic of my former self, I would seclude myself and feel very remorseful for the act. . . . That awful, awful despondency and depression I shall never forget. . . .

[When] the back of my hands became very red and the above symptoms of the nerve system were gradually getting worse, . . . I realized that I had that "condition" called pellagra. I immediately . . . prepared to die. I had lost in weight sixty pounds.

Dr. Haynes's life was saved by the administration of a proper diet, rich in the vitamins he lacked, and with a general toning up of the nervous system, he resumed the practice of medicine.

This is the story of the modern, twentieth century Job, inscribed in a book, with a modern pen, for the sake of the suffering, . . . that [physicians] do not

deal with pellagra lightly, or say that one is hysterical and imagines this, that or the other thing, but to go deep down into the very foundation and find the cause, have patience, sympathy, and plenty of time for the study of each patient.[7]

Now let me turn to the Book of Job in the Old Testament.

Job was a happy man, a man of wealth, with a healthy family about him, more sons than daughters (sons being more esteemed than daughters), large numbers of cattle and work animals, rich pastures and a beautiful home of his own. By a cruel blow of fate, according to the Book of Job, misfortune suddenly came to him. One stroke followed another; his houses were destroyed; he lost his possessions, and, as a result, his health suffered. He was stricken with a serious illness, gradual in its development, breaking out first in one part and then in another; by degrees the entire body became involved. He shunned his friends, his sole refuge being in the village dunghill or refuse heap, the only resting place of outcasts who, stricken with some loathsome disease, were excluded from the dwelling places of man. Three friends came to visit him and tried to comfort him and to encourage him to hope for recovery. His lamentations—beginning with the first cry of misery, "Would to God I had never been born"—and his deep philosophic expositions are not for this dissertation. Every human being should familiarize himself with this great book of the Bible. The medical condition of Job is the subject of this discussion.

Job was suffering from an acute, overwhelming disease that began with a severe inflammation of the skin, extending over his entire body "from the soles of his feet to the crown of his head." A generalized itch (pruritus) accompanied this condition. "He took him a fragment of a clay vessel to scratch himself with, and he applied mud to the involved areas," which cooled the severe burning and itching caused by the dermatitis.

"This skin lesion," remarked Job, "has taught me the value of the application of mud." He covered his entire body with a thick layer of mud, which made him feel as if he "really wore nothing but earth." The skin was soon filled with sores which crusted and formed the breeding places of maggots; these sores broke down and discharged profusely. His face became so swollen (cellulitis) and disfigured that his friends could not recognize him. In the midst of his sufferings he appealed to the Lord: "Thy hands have fashioned and created me, yet Thou permit me to be covered with the processes of decomposition that will utilmately destroy me." He described the appearance of his skin as "a moth-eaten garment that covers a worm-eaten and decomposing body."

The pain that accompanied these lesions was so intense and so agonizing that his wife, who could not bear the poor man's suffering, prayed that her husband "be spared such agony by instantaneous death." The

pains were so severe that at times he could scarcely "catch his breath." Luckily for the patient the pains were paroxysmal, with periods of slight relief.

He could not sleep through the night. He was "exhausted from the tossings to and fro even until the dawn; before the day is done it is night again—the light is too close to the darkness." He became prostrated from the lack of sufficient sleep. The little that he did get was "troubled by dreadful dreams and the most terrifying visions," so that his "soul chose strangulation or any other form of death rather than continue residing in the skeleton to which he had been reduced."

His skin began "to wrinkle," and soon the "emaciation was pronounced; his bones stuck to his skin." The gums, called "the skin of his teeth," were the only parts of his body that escaped emaciation. "My garment (skin)," he wailed, "is changed. From a normal, elastic tissue, it is now become taut, and acts like a vise that is constricting me" ("it bindeth me about as the collar of my shirt"[8]). His body wasted to such an extent that he felt "as light as a feather"; his weakness caused him to become "languid and slow of movement."

His abdomen sank in as a result of the wasting of the abdominal fat, so that intestinal peristalsis became visible. "My intestines boil and cannot remain silent," he wailed. Another complaint was severe backache: "archers shot their darts at me which split my kidneys." His temperature was high: "my bones are charred from the fever." The pigmentation of his skin was explained by Job in these words: "I have become bronzed; my skin is black upon me, not from the sun, but from the internal heat that consumes me."

As he became "a shadow of himself" his "vision began to fail" and his eyes lost their luster, "the shadow of death hovers about my eyelids," he lamented. Then followed fainting spells and attacks of cardiac palpitation (according to Rashi's interpretation of the passage, "his soul pours itself out"):

"My disease is more serious than the symptoms warrant," Job cried, and he pleaded with his friends that they "determine the cause (*shorash*) of his illness."

The possibility of a venereal origin troubled him, and he chided himself for some imaginary transgression of his youth. "Thou hast made me inherit the sins of my youth," he cried out to Yahweh. He was led to this belief by the fact that during his illness he had become impotent: "my desire for my wife is alienated from me." Had he not "made a covenant with my eyes not to even think of a maid? My heart was never enticed by a woman; upon no man's doorstep did I ever lurk (adultery); if such ever were the case then let strange men do the

8. Job 30: 18.

same to my wife." No, he never did commit such a sin, for it was carnal and lewd. He compared the consequences of illicit sexual congress with his own sick state: "For such a sin the punishment is a loathsome and suffering sickness; adultery is a crime which is like a fire, spreading and consuming until the criminal is destroyed, and all his possessions are gone."

For ages Job's illness was confounded with syphilis, leprosy and other "loathsome" conditions. But the story ends with Job's cure. "All his brothers and all his sisters and all his old friends came to celebrate his recovery, and to feast with him at his home; and they brought him many gifts. And Job was healthier after his recovery than ever before in his life. He regained his reproductive powers and begat seven sons and three daughters—the most beautiful girls in all the surroundings. After his terrible illness he lived to a ripe old age—140 years—unto the fourth generation of grandchildren. And Job died a very old man, enjoying every day of his remaining years."

The Biblical account compares with modern observations of pellagra. One does not fail to recognize the similarities in the two case histories, the complaints of the ancient Job and of the modern Job.

The painstaking and detailed description of Job's illness in the Old Testament is that of a disease that must have been prevalent among the impoverished peasants of those days; for it was only after Job had lost all his possessions and riches and was reduced to a lowly state that the signs and symptoms so characteristic of the disease now recognized as pellagra developed.

The Corpus Hippocraticum, which is attributed to Hippocrates, the father of medicine, and which is a compilation of the most detailed case histories (without diagnosis), does not contain even one that can compare with the Biblical description of pellagra.

The modern appellation of this disease is pellagra, from *pellis,* skin, and *agra,* catching. In the days of the ancient Hebrews it was termed *sh'chin raa,* the evil skin disease! After all, what's in a name?

CLINICAL EVALUATION OF A SUPERFATTED SOAP

ROY L. KILE, M.D.
CINCINNATI

In 1885 Paul Unna the elder proposed to ameliorate the occasional deleterious effects of soap on the skin by using more fat than was required to neutralize the alkali employed in its manufacture. This superfat, it was reasoned, would eliminate the possibility of free alkali remaining in the finished soap and might even combine with the alkali formed by hydrolysis when the soap was dissolved in water.

The concept that the irritating and drying actions of soaps on the skin are dependent only on their alkaline reaction is no longer held. Soaps of fatty acids with a short carbon chain (i. e., low molecular weight), which hydrolyze least [1] and are therefore least alkaline, have been found to be most irritating to the skin.[2] Also in this connection, Bleyberg and Lettner [3] have concluded that the presence in soap of a few tenths of 1 per cent of free alkali has little if any influence on the p_H of its solution.

From the formulas of several superfatted soaps available on the market today, it appears that the ability to counteract alkalinity is not considered to be of primary importance. Most of these soaps are superfatted with hydrous wool fat or one of its derivatives or with a wax, none of which has great power to neutralize alkali, or with a paraffin, such as petrolatum or liquid petrolatum, which has none. The use of these materials in soap seems to be directed toward decreasing its defatting effect on the skin rather than toward counteracting its alkalinity.

Soaps containing large proportions of superfat do not lather well; for this reason such soaps are not always satisfactory for general use. In formulating soaps of this type, manufacturers have evidently added as much superfat as possible while still maintaining lathering ability at a desirably high level.

1. Lustig, B., and Schmerda, F.: Zur Hydrolyse der Natriumseifen in wässriger Lösung, Fette u. Seifen **44**:51, 1937.

2. Emery, B. E., and Edwards, L. D.: The Pharmacology of Soaps: II. The Irritant Action of Soaps on Human Skin, J. Am. Pharm. A. **29**:251, 1940. Blank, I. H.: Action of Soap on Skin, Arch. Dermat. & Syph. **39**:811 (May) 1939.

3. Bleyberg, W., and Lettner, H.: Die Alkalität verdünnter wässriger Seifenlösungen und ihre Beeinflussung durch Zusätze freien Alkalis, Chem. Umschau a. d. Geb. d. Fette, Oele, Wachse u. Harze **39**:241, 1932.

The question then arises as to whether such superfatted soaps are of value. A survey of the literature discloses the fact that there is considerable disagreement among clinicians as to the advisability of using these soaps.

The late Dr. Pusey [4] has written:

When, however, it is desired to overcome completely the effect of the alkali, soaps are superfatted, as it is called, by the addition of about one per cent of lanoline, a fat which does not become rancid. These superfatty soaps are the least irritating of soaps and are little, if at all, less efficient for cleansing the skin than ordinary toilet soaps. When soaps are for any reason badly borne by the skin, these superfatted soaps are useful, although such refinement in soaps is not necessary for the ordinary individual.

Similarly, according to Stillians,[5]

Superfatted soaps, in which the addition of a small percentage of wool fat has overcome entirely the action of free alkali, are the least irritating soaps. Greasy skins stand soaps well and only very dry skins need to be protected by the use of superfatted soaps or the avoidance of soaps entirely.

On the other hand, Klauder, Gross and Brown [6] stated:

Superfatting agents have little influence after hydrolysis of soap. We believe that superfatted soap has been unduly emphasized as a toilet soap.

While indicating that superfatted soaps may be less drying to the skin, Parkhurst [7] stated the belief:

The use of superfatted or olive oil soaps which leave an oily residue even in distilled water does not seem advisable.

He suggested further:

A bland oil may be applied to the clean skin after washing if the skin tends to chap.

On this subject, Swartz and Reilly [8] stated:

Superfatted soaps are those which contain fatty acids in excess of that required to unite with the alkali used. If this excess is more than a fraction of a per

4. Pusey, W. A.: The Care of the Skin and Hair, New York, D. Appleton-Century Company, Inc., 1936, p. 74.

5. Stillians, A. W.: Notes on the Care of the Skin, Illinois M. J. **43**:388, 1923.

6. Klauder, J. V.; Gross, E. R., and Brown, H.: Prevention of Industrial Dermatitis, Arch. Dermat. & Syph. **41**:331 (Feb.) 1940.

7. Parkhurst, H. J.: Toilet Soaps, Soap Substitutes and Hard Water, Arch. Dermat. & Syph. **43**:299 (Feb.) 1941.

8. Swartz, J. H., and Reilly, M. G.: Diagnosis and Treatment of Skin Diseases, New York, The Macmillan Company, 1935, p. 19.

cent, the efficiency of the soap is thereby lessened. On the whole it would seem that "superfatted," as applied to many soaps, is a meaningless term.

It has been my experience that patients with dry skins definitely prefer to use a superfatted soap. It then becomes important to know whether the reason for this is real or psychologic, i. e., whether there is an objective difference between superfatted and ordinary toilet soaps in their effects on the skin.

The following experiment was planned to give an answer to this question.

Fifty-seven young women (nurses) were divided, without selection, into two groups. One group was given a supply of plain stamped bars of ordinary toilet soap, while the other received a superfatted soap of similar appearance. The soaps were made from the same stock, having a fat formula similar to that of a high grade toilet soap, and

TABLE 1.—*Results for Entire Group (Fifty-Seven)*

Patients' Appraisal of the Soap	Control Soap	Superfatted Soap	No Difference Noticed
Discomfort experienced	6	1	50
Increased dryness of the skin	31	9	17
Improvement in acne	7	0	50
Better lathering qualities	15	9	33
Preference	22	27	8

both contained the same kind and amount of perfume. The only difference was that 1.5 per cent of hydrous wool fat had been milled into the superfatted soap. This formula is comparable to formulas for superfatted soaps available on the market.

Each group used the soap supplied for two weeks. At the end of this time, the group which had been using the control soap was given the superfatted soap, while the other group was furnished with control bars. The subjects had no knowledge of what the difference in the two soaps might be.

Weekly examinations of the subjects were made to determine whether there were any objective effects of the soap on the skin. The face, hands and arms were observed for any indication of irritation, for the presence of acne and for the general condition of dryness or oiliness of the skin. At the same time each subject was questioned with regard to her own appraisal of the soap, with particular reference to discomfort

experienced, the condition of the skin (dryness and acne) and the lathering qualities of the bar. At the conclusion of the second experimental period, each subject was asked to give her preference of the two types of soap.

The test was conducted during the winter season, when the temperature and humidity were low and when dry, chapped skins were not unusual. Since a considerable change in the weather from one two week period to the next might conceivably influence the results, a record was kept of the average daily temperatures. These varied from day to day, but the grand average of the daily average temperatures was the same (32 F.) for the two experimental periods.

The results for the entire group are presented in table 1, while those for the subjects who had definitely dry skins are given in table 2, for purposes of comparison.

TABLE 2.—*Results for Twenty-Nine Subjects with Dry Skins*

Patients' Appraisal of the Soap	Control Soap	Superfatted Soap	No Difference Noticed
Discomfort experienced	5	0	24
Increased dryness of the skin	17	4	8
Improvement in acne	3	0	26
Better lathering qualities	8	4	17
Preference	5	18	6

COMMENT

If the two soaps had been identical or the difference too slight to be discernible, the subjects would, according to the laws of probability, have been divided approximately equally in their opinions of the drying and other properties of the two soaps.

From the tables, however, it appears that there was a true difference between the soaps in their effects on the skin. The evidence indicates that more discomfort was experienced during use of the control soap than during use of the superfatted product. It is interesting to note in this connection that most of the subjects who reported discomfort with the use of either soap had dry skins.

Further, dryness of the skin was noted in more subjects during use of the control soap than during use of the superfatted soap. This ratio is 3 to 1 for the entire group and 4 to 1 for the group with dry skins.

A few subjects noted some improvement in their acne while using the control soap and none while using the superfatted bar. The lathering properties of the superfatted soap were less satisfactory than those of the control; the latter gave a greater abundance of lather, although it was less creamy.

Subjects with dry skins showed a definite preference for the superfatted soap, while those with normal or oily skins preferred the control bar. From the results of this test, it would appear that an average group of women, selected at random, would not, as a group, have a distinct preference for either of the two types of soap.

Whether a superfatted soap of this kind acts by removing less oil from the skin than does ordinary toilet soap or by leaving a residue of its superfat on the skin has not been demonstrated. A study to answer this question is planned.

SUMMARY

In a practical usage test on young women, two soaps, identical except for superfat content (one soap containing 1.5 per cent of hydrous wool fat), were compared during cold weather, with the following results:

Eighty-six per cent of the subjects noted no discomfort, drawing or burning with either soap.

Twelve per cent noted some discomfort with the control soap.

Two per cent noted some discomfort with the superfatted soap.

Thirty per cent observed no difference in the drying effect of either soap.

Fifty-four per cent found the superfatted soap less drying than the control soap.

Sixteen per cent found the control soap less drying than the superfatted soap.

1219 Carew Tower.

Clinical Notes

LICHEN PLANUS CONFINED TO THE ORAL CAVITY IN TWINS

Report of a Case

STEPHAN EPSTEIN, M.D., MARSHFIELD, WIS.

Familial lichen planus is rare. As far as I can see its occurrence in twins, as presented here, has not been reported in the literature.

REPORT OF CASE

V. S., a white man, born Aug. 31, 1914, was first seen at the office on Jan. 13, 1939. He had noticed white lesions in the mouth about two months previously.

Examination revealed typical lichen planus confined to the oral cavity. Numerous confluent reticular lesions covered nearly all of the mucous membranes of the cheeks. On the left side of the tongue, two oval annular lesions were present, unnoticed by the patient. The lips were not involved. No other lesions were found.

The results of urinalysis and a blood count were normal, and the Wassermann reaction of the blood was negative. Six months later, after the intake of 60 cc. of solution of potassium arsenite U. S. P., the eruption cleared up except for a few lesions. The patient then received vitamin B complex. He claimed that he was "getting along fine and feeling good" as long as he kept on taking the capsules, but when he stopped the lesions in his mouth recurred.

R. S., the twin brother of V. S., first consulted me on Feb. 20, 1941. About August 1940 he noticed lesions on the middle of the tongue and the mucous membrane of the cheeks, which grew steadily worse. Later a lesion appeared on the lower lip. The similarity of the eruption in the brothers was so striking that the patient himself made the correct diagnosis. The general history was irrelevant except that he was run down at the time the eruption appeared; he stated that he had been "running around quite a bit" prior to his marriage in September 1940.

Examination revealed a picture of lichen planus similar to that of his brother. The lesions covered nearly all of the mucous membrane of the cheeks. The lesion of the tongue apparently had disappeared by that time, but the right side of the lower lip presented a typical annular lesion about 9 by 6 mm.

The results of urinalysis and a blood count were normal, and the Wassermann reaction of the blood was negative. The patient was treating himself with vitamin B complex, up to 9 capsules a day. According to his report, his condition has improved greatly.

COMMENT

This case is interesting in the following respects:

1. The patients were twins, and to all outward appearances identical twins.

2. No other members of the family were affected; neither the parents, with whom the twins lived at the time of the outbreak of the eruption, nor an older brother, who worked with them, had this condition.

From the Marshfield Clinic.

3. There was a definite nervous element. Both patients were nervous and high strung. They owned a clothing store; the business was satisfactory, but they believed that they had to hurry and worry all the time to keep things going. Both brothers realized the relation of their dermatosis to their nervous status; they expressed the opinion that they were much better when they stopped worrying and getting excited. There was furthermore the history of additional nervous strain in one brother (R. S.).

4. The clinical lesions of the two patients were nearly identical. Only the oral cavity was involved. The mucous membranes of the cheeks were covered almost completely. The lesions of the tongue and of the lip were annular. The involvement of the lip in the second patient (R. S.) constituted the only difference.

Similarity of symptoms in cases of familial lichen planus has been reported relatively frequently, probably too often to be considered a coincidence. Little's observation[1] of lichen planus confined to the mucous membranes of the mouth in mother and son corresponds to the cases reported herein. These observations are of interest because they may give an etiologic clue, indicating either a familial disposition or special qualities of the causative agent—if lichen planus is an infection at all. It seems to me that the observations in my report point in both directions. The identity of the sites of the lesions and the fact that only the twins were affected favor a special disposition, whereas the time relation favors the infectious theory.

1. Little, cited by Juliusberg, F.: Lichen ruber und Pityriasis rubra pilaris, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 7, pt. 2, p. 116.

DERMATITIS CAUSED BY TAR PAPER STORAGE BAGS

Report of Two Cases

LESTER HOLLANDER, M.D., PITTSBURGH

CASE 1.—K. K., a 50 year old merchant, was examined on account of an indefinite fine vesiculoerythematous eruption which appeared on his legs and on the lower part of his thighs, an area left uncovered by his shorts and socks. The eruption caused intolerable itching, which was most pronounced during the day, especially when he was sitting. He first noticed it about the beginning of October 1939.

It was apparent that this eruption had something to do with his trousers, but the exact cause remained undetermined. Wool, cleaning fluids and dyes were easily eliminated as factors.

Topical application of calamine lotion containing 0.5 per cent of menthol caused amelioration of the symptoms, but recurrences of the eruption persisted until the end of December 1939, when they ceased without any determined reason.

Early in October 1940 he returned presenting a similar eruption. The cause remained obscure until examination of another patient brought new light on the subject.

From the Pittsburgh Skin and Cancer Foundation.

CASE 2.—T. B. O., a 16 year old school boy, was examined on account of an indefinite fine vesiculoerythematous eruption which affected his legs and the lower portion of his thighs. These spotty areas of eruption were observed only on that portion of the skin of the lower extremities with which his trousers came in direct contact, areas left uncovered by his shorts and socks.

The eruption began some time after Labor Day 1940 and persisted for about two months. Itching was intense and more severe during the day.

Questioning elicited the fact that he had changed to heavier than summer trousers after Labor Day and that these had been stored during the summer in tar paper bags. Patch tests with material from the inner surface of such a storage bag yielded strongly positive evidence that it was the cause of the dermatitis. Most of the vesiculoerythematous areas on his legs became more noticeable during and shortly after the patch tests.

All of the trousers stored in these bags were turned inside out, well aired and then dry cleaned. The eruption disappeared in about fourteen days.

Similarity to the condition in case 1 was so noticeable that it was no surprise when the institution of the same procedures in this case resulted in the disappearance of the eruption.

There was no recurrence of the eruption the following fall in either patient (their clothes were stored in cedar chests during the summer).

631 Jenkins Building.

Obituaries

HOWARD MORROW, M.D.

1874-1941

Howard Morrow died at his home, in San Francisco, on Wednesday afternoon, Oct. 22, 1941, of a heart attack. The end, sudden and unexpected, was a shock to his relatives, friends and colleagues. In June 1938 Dr. Morrow had a cerebral attack while attending the annual meeting of the American Dermatological Association in Del Monte, Calif. Fortunately, the attack was mild and was followed by rapid and complete recovery. At this time Dr. Morrow wisely reduced his strenuous activities, but he did attend the annual meetings of the Association in Eastern Canada, in 1939, and at Colorado Springs, Colo., in 1940. He appeared to be enjoying the best of health, and at the latter place he joined an automobile party on a trip to the summit of Pike's Peak. He missed the 1941 meeting at New Orleans, but this was for reasons other than poor health.

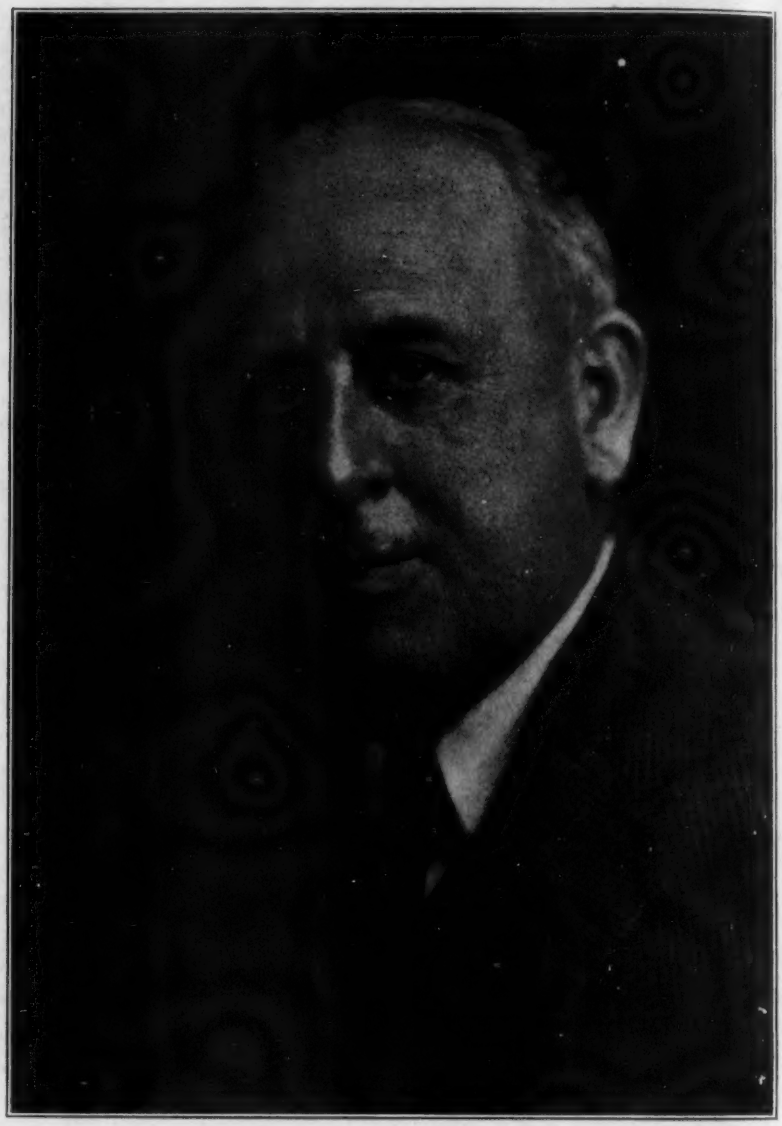
Dr. Morrow was born in San Francisco on Nov. 12, 1874. His father, a miner and rancher, was Robert Fulton Morrow and his mother, Eliza Gummer Morrow. There were three brothers, none of whom entered the medical profession.

Dr. Morrow's premedical education was obtained at Stanford University (1891-1892). He graduated from the University of California Medical School in 1896 and was licensed by the state of California the same year. He spent the next five years studying dermatology and syphilology in New York, London and Vienna. He opened an office and began the practice of dermatology and syphilology in San Francisco in 1901.

Dr. Morrow married Mary Weldon on Dec. 24, 1900. Most dermatologists in this country know and admire the gracious and talented Mrs. Morrow; she has their deepest sympathy. The happy couple were blessed with four children, one girl and three boys, one of whom is now a physician.

Dr. Morrow was made clinical professor of dermatology at the University of California Medical School in 1911. He held this title and was director of the department of dermatology until a year or two before his death. He was chairman of the Section on Dermatology and Syphilology of the American Medical Association in 1915, president of the American Dermatological Association in 1918 and vice president

of the American Medical Association in 1938. He was president of the California Medical Association in 1937 and president of the California State Board of Health from 1933 to 1940. He was a member of



HOWARD MORROW, M.D.
1874–1941

the California Academy of Medicine and of the London, French and Vienna medical associations. He was a charter member of the American Board of Dermatology and Syphilology and served it faithfully and well

until his resignation, in 1938. He was consulting physician to the United States Marine Hospital and the United States Public Health Service.

Dr. Morrow was a busy, hard-working physician. He had a large private practice and a large service at the University, in spite of which he found time to participate in many state and national professional activities—dermatologic, educational and political. He was not an orator, but he was an excellent teacher, and when he had anything to say he was a good speaker. He had a scientific mind, but he never entered deeply into the research field. He was a superb clinician and a fine physician. He was not a prolific writer, but his two dozen or more contributions were carefully done and they deserved the respectful attention that they received. Morrow never wrote or spoke professionally unless certain that the subject was worth presenting.

Dr. Morrow was a big, healthy-looking man physically. He was "big" in every way. He had a jovial disposition, a fine sense of humor and an engaging personality. He was endowed with an unusual amount of common sense. He was capable of being guided and of guiding and was very loyal. He was a fine friend to have. He was sociable and sociably inclined. He was a member of the Olympic Club, the University Club, the delightful Family Farm and many other social organizations. He enjoyed the theater, music and a good dinner with congenial friends. He had many hobbies, which would have kept him interested and occupied in case of retirement.

Surviving Dr. Morrow are his widow, Mary Weldon Morrow; his recently married daughter, Mrs. Maryle Doerflinger; three sons, Weldon, Robert and Dr. Grant Morrow, and a brother, William G. Morrow, all of San Francisco.

Dr. Morrow's death is a great loss to American dermatology; he will be sadly missed by all who were fortunate enough to know him.

GEORGE M. MACKEE, M.D.

Appreciation

ARMAUER HANSEN
1841–1912

REIDAR MELSON, M.D.
Physician in Chief, Bergen Leprosorium
BERGEN, NORWAY

On July 29, 1941 a century had passed since Gerhard Henrik Armauer Hansen, the discoverer of the lepra bacillus, was born at Bergen, Norway. The discovery of this organism is justly considered the most important medical event which has taken place in Scandinavia. The real significance of Hansen's contribution to medicine in general and to bacteriology in particular can be fully grasped only when one recalls the position investigative medicine had reached in 1873, when the lepra bacillus was discovered. It is true that the anthrax bacillus and certain pathogenic fungi were already known and that the Norwegian physicians Winge and Heiberg had demonstrated streptococci in the heart valves in a case of fatal septicemia. It is also true that Obermeier had discovered the spirochete of relapsing fever in 1868, although this discovery was first published in 1873, almost simultaneously with that of the lepra bacillus. But these sporadic findings were not generally recognized. It is certain, however, that no bacterium had been associated with any chronic disease, as the causative agent, before Hansen's discovery of the lepra bacillus. Pasteur's revolutionizing investigations on human pathogenic micro-organisms appeared subsequent to Hansen's discovery. Koch isolated the tubercle bacillus nine years afterward (1882), and it was at the turn of the century, in 1905, that Schaudinn and Hoffmann discovered Spirochaeta pallida in syphilis. These facts make Hansen's discovery of the lepra bacillus in 1873 so much more remarkable.

In the middle of the nineteenth century leprosy presented a serious problem in Norway. As a young physician, in 1868, Hansen became affiliated with the lepra hospitals at Bergen. His remaining years were entirely and unceasingly dedicated to scientific and practical work with leprosy. As he had lived, so he also died in the midst of his work for the Norwegian lepers, on an inspection tour in 1912 to lepers hospitalized in the country.

Hansen's discovery of the lepra bacillus was not a mere coincidence. As a young physician he had studied and assimilated the new and

Part of an address at the Centenary of Hansen's birth, recently celebrated in Bergen, Norway.

revolutionizing ideas which dominated bacteriologic, medical and biologic thought during the middle of the nineteenth century. Thus he wrote: "In this fungus-mad epoch, as Cohnheim calls it, my own investigations must necessarily follow in the self-same direction." When one recalls that the technic of staining bacteria was exceedingly primitive at the time, one must not expect Hansen to have rendered a more adequate description of the lepra bacillus than he did in 1873. He described the bacilli as "rods lying clumped together in bundles and crossing each other at very sharp angles." In his "Investigations Concerning the Causes of Leprosy" he was not content to render a histologic demonstration of the bacillus. He also furnished incontrovertible clinical and epidemiologic proof that the disease was contagious rather than hereditary. The latter was the general opinion held by experts at that time.

In 1875 Hansen was made physician in chief for all the lepers in Norway. In this capacity he became the driving force behind all public health efforts to combat the disease. "The law about the care of indigent lepers, etc." of 1877, subsequently revised in 1885, was due mainly to his efforts. This law put into effect the principle of compulsory isolation. The results of the governmental precautions enforced for the lepers in Norway have been so noteworthy that these precautions have served as a pattern for many other countries. Thus the number of lepers in Norway has been reduced from approximately 3,000 in 1854 to 25 in 1941.

Hansen was not solely preoccupied with leprosy. He was also an accomplished biologist, serving in this capacity on the staff of the Bergen Museum. He was an ardent follower of Darwin's theory of evolution, which he endeavored to popularize. Through these efforts he earned the displeasure of the church and was bitterly assailed by the clergy.

He shared the fate of other great minds who labored in advance of their time and was met with opposition and lack of recognition. Another contemporary great Norwegian leprologist, D. C. Danielsen, had already won international renown, and Bergen had become a center for investigations in leprosy.

Hansen received during his lifetime the international recognition which he justly deserved. At the First International Lepra Congress, held in Berlin in 1897, he was unanimously declared to be the discoverer of the Mycobacterium leprae. It was his misfortune to have discovered a micro-organism which even today defies all attempts at artificial cultivation. Thus he was robbed of the chance to carry on more intensive biologic investigations of the bacillus which is always present in leprosy. But his numerous contributions to leprology coupled with his discovery of the lepra bacillus will always be held in reverent esteem in the history of medicine.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

EFFECT OF ULTRAVIOLET IRRADIATION OF AIR ON INCIDENCE OF INFECTIONS IN AN INFANTS' HOSPITAL. FE DEL MUNDO and CHARLES F. MCKHANN, Am. J. Dis. Child. **61**:213 (Feb.) 1941.

The dermatologist who may be called into consultation regarding the elimination of impetigo of newborn infants in hospital nurseries should consult this article.

TOXIC EFFECTS WITH ANURIA FROM A SINGLE INJECTION OF A BISMUTH PREPARATION: REPORT OF TWO CASES. S. J. MCCLENDON, Am. J. Dis. Child. **61**:339 (Feb.) 1941.

McClendon presents 2 cases in which anuria developed following a single injection of a bismuth preparation. This drug was used in the treatment of acute Vincent's gingivostomatitis. In both cases the patients were infants and the dosage of bismuth employed was five or six times the usual dose. The type of bismuth used was not given. Recovery followed the intravenous and hypodermic administration of fluids and blood transfusions.

INFECTION OF SCALP AND CILIA WITH PHTHIRUS PUBIS IN A NINETEEN MONTH OLD BABY. LEON GOLDMAN and LEO S. FRIEDMAN, Am. J. Dis. Child. **61**:344 (Feb.) 1941.

Involvement of the eyelashes with Phthirus pubis is not uncommon. Infection of the scalp with the pubic louse is, however, extremely rare, there being only 10 cases reported in the foreign literature. The authors report the case of a 19 month old baby in whom the scalp and eyelashes were involved.

STURGE-WEBER SYNDROME: ITS OCCURRENCE IN TWO CASES. JOHN WISTER HAINES and GORDON HUGHES PUMPHREY, Am. J. Dis. Child. **61**:557 (March) 1941.

In this syndrome there occur vascular nevi along the course of the superior and middle branches of the trigeminal nerve, glaucoma of the eye on the same side and vascular nevi of the pia. Thus there is a congenital mesodermal anomaly involving the vessels of the pia, choroid and skin. In the present report of 2 cases emphasis is placed on the primary importance of the presence of the pial nevus in identifying this syndrome.

OSTEITIS FIBROSA CYSTICA (ALBRIGHT). JAMES LOCKE NELLER, Am. J. Dis. Child. **61**:590 (March) 1941.

In 1937 Albright and his co-workers presented 5 cases in which a peculiar syndrome was present. This syndrome was characterized by osteitis fibrosa cystica, areas of cutaneous pigmentation and endocrine dysfunction with premature puberty in female patients. The areas of pigmentation were flat, patchy and light brown. They were not unlike the café au lait areas of macular pigmentation seen in von Recklinghausen's neurofibromatosis. They tended to occur on the buttocks, in the sacral and lumbar regions and on the back of the neck. The amount of pigmentation was roughly proportional to the severity of the osseous lesions and tended to occur on the same side of the body or on both sides if the bony lesions were widespread. The present report adds an additional case to the 23 cases already reported.

APHTHOUS PHARYNGITIS. B. B. BREESE JR., Am. J. Dis. Child. **61**:669 (April) 1941.

In the summers of 1938 and 1940 the author encountered 28 cases of an unusual type of pharyngitis. There was an incubation period of about three days followed by a sudden high temperature, mild subjective symptoms and inflammation of the soft palate and tonsillar pillars together with the appearance of aphthous lesions in the same areas. The symptoms generally last only twenty-four hours, although it may take several days for the lesions in the throat to disappear entirely. The cause of the disease is unknown.

HAND-SCHÜLLER-CHRISTIAN DISEASE: A CASE IN WHICH LYMPHADENOPATHY WAS A PREDOMINENT FEATURE. MARGIT FREUND and MAURICE L. RIPPS, Am. J. Dis. Child. **61**:759 (April) 1941.

This is an extensive case report of a variant of the usual clinical picture of Hand-Schüller-Christian disease. In this instance lymphadenopathy was the first and chief symptom and appeared at the early age of 7 weeks. Typical osseous changes occurred at the age of 13 months. There were no cutaneous lesions. The diagnosis was confirmed by autopsy.

THE DISTRIBUTION OF PIGMENTATION ON THE ARM AND THORAX OF MAN. PALMER HOWARD FUTCHER, Bull. John Hopkins Hosp. **67**:372 (Nov.) 1940.

In about 17 per cent of 200 Negroes Futcher has found a peculiar distribution of pigmentation in the anterior deltoid region of the arm. There is a sudden transition in the degree of cutaneous pigmentation in this area. In a Negress whose photograph is given this pigmented line also extended across the thorax at about the level of the third rib.

DURATION OF INFECTIVITY OF TREPONEMA PALLIDUM IN CITRATED BLOOD STORED UNDER CONDITIONS OBTAINING IN BLOOD BANKS. THOMAS B. TURNER and THOMAS H. DISEKER, Bull. Johns Hopkins Hosp. **68**:269 (March) 1941.

In a series of experiments the authors have shown that under conditions obtaining in blood banks, Spirochaeta pallida undergoes progressive deterioration in citrated whole blood during the storage period. There is a corresponding reduction in the risk of transmitting syphilis by transfusion, and it is probable that blood stored for four days or longer can no longer transmit this disease.

MULTIPLE SELF-INFLICTED SUBCUTANEOUS ABSCESSES: CASE REPORT. ARTHUR KLEIN, Bull. Johns Hopkins Hosp. **68**:409, 1941.

In an interesting report, Klein details an instance of dermatitis factitia in which the self-produced lesions were subcutaneous abscesses requiring incision and drainage. They were apparently produced by the hypodermic injection of a purulent fluid.

LOSS OF VIRULENCE OF TREPONEMA PALLIDUM IN CITRATED BLOOD AT 5° C. OSCAR BLOCH JR., Bull. Johns Hopkins Hosp. **68**:412, 1941.

The introduction of blood banks in most large metropolitan hospitals has largely replaced the use of fresh, whole or citrated blood for transfusions. Since transfusion syphilis has occurred with direct or immediate indirect transfusions, it became essential to know the survival time of Spirochaeta pallida in blood stored in blood banks. Using rabbits as the experimental animal, Bloch determined that there was a definite risk of transmitting syphilis to the recipient of blood from patients with early syphilis if the blood had been preserved for seventy-two hours or less in the blood banks. Even though this risk apparently diminishes rapidly after ninety-six hours, it is still unwise to use the blood from persons with syphilis known to be in an early stage. NELSON PAUL ANDERSON, Los Angeles.

IRRADIATION IN DERMATOLOGY. ANTHONY C. CIPOLLARO, Radiology **36**:684 (June) 1941.

After forty years' experience with roentgen rays and radium, there is still a lack of uniformity of dosage. The correlation of the histologic pictures of many dermatoses and the depth dosage of roentgen rays of varying wavelengths has received little or no attention. Absorption curves obtained with kilovoltage of 40 to 100 indicate that good results should be obtained with the lower voltages as well as with the higher, using the same number of roentgens on the surface of the skin. High voltage and heavy filtration have no place in dermatology.

To treat cutaneous diseases properly with roentgen rays, the physician should be familiar with the physical factors as well as with the natural course of the disease. Therefore one trained only in radiology or one without training but owning an x-ray apparatus and equipped with knowledge given him by a salesman cannot properly treat cutaneous diseases.

A group of cutaneous diseases that are commonly treated with roentgen rays are discussed. It is emphasized that irradiation is not the only method of treatment. The chart showing absorption curves is most instructive and useful. The plea for uniformity in dosage which promises better therapeutic results and greater safety to patients is emphasized in several places in the paper.

AUTHOR'S ABSTRACT.

THE ROENTGEN TREATMENT OF MYXOMATOUS CUTANEOUS CYSTS. HAROLD W. JACOX and LESTER J. FREEDMAN, Radiology **36**:695 (June) 1941.

The authors report 7 cases of this disease, which has at times been miscalled synovial lesions of the skin, with clinical and histologic descriptions of the disease and illustrations. Every patient was cured with a single dose of roentgen rays after the optimal dose was found. One patient did not complete the treatment, but with radiation short of the caustic dose recommended the lesion improved.

The physical factors employed were as follows: 100 kilovolts constant potential, 4 milliamperes, 30 cm. focal skin distance, no added filtration, intensity 120 r per minute, portal size as determined by the lesion 1,400 r to 1,600 r, closely shielded and massive dose technic (one sitting). Regression of the cyst occurred in from four to twelve weeks.

AN OINTMENT FOR THE RELIEF OF DISCOMFORT DUE TO SEVERE IRRADIATION EPIDERMITIS. HOWARD HICKS ASHBURY, Radiology **36**:739 (June) 1941.

For the relief of pain following severe reaction to roentgen irradiation of the skin and mucous membranes, the author recommends several applications a day of an ointment made of 0.5 to 1 per cent tetracaine (parabutylaminobenzoyldimethylaminoethanol hydrochloride) in an oxycholesterol-petrolatum base.

ROENTGENOGRAPHIC DIAGNOSIS OF VERTEBRAL SYPHILIS. MAX SGALITZER, Radiology **37**:75 (July) 1941.

Three cases of vertebral syphilis affecting the cervical vertebrae are described. The roentgenographic changes are so characteristic that they can be readily differentiated from those of other diseases affecting this region. The author emphasized the point, that even though the vertebral bodies had undergone extensive destruction, there was a complete absence of collapse due to pronounced sclerosis and hyperostosis.

CIPOLLARO, New York.

FAMILIAL VULNERABILITY OF SPECIAL SITES TOWARDS THE LESIONS OF CONGENITAL SYPHILIS: ISCHEMIC DISTURBANCE IN FINGERS OF TWO SISTERS, PROBABLY DUE TO THIRD GENERATION SYPHILIS. T. ANWYL-DAVIES, DAVID NABARRO and F. PARKES WEBER, Brit. J. Child. Dis. **37**:173 (July-Sept.) 1940.

The mother of the 2 girls was known to have latent untreated syphilis (probably congenital). Both girls had signs of "commencing gangrene" of the fourth and

fifth terminal digits of the right hand soon after birth. The elder child's condition gradually healed with scarring, and the Wassermann and Kahn reactions were negative. The younger child was seen during the active stage of the condition, and her serologic reactions were positive.

LANGMANN, New York. [AM. J. DIS. CHILD.]

ULCERS OF THE LEG. JORGE MILLAN GUTIERREZ, Prensa méd. mex. **60**:75 (June) 1941.

The author stresses the frequent absence of varicosities in so-called varicose ulcers and discusses the etiologic features of ulcers of the leg, such as heredity, predisposition and endocrine, inflammatory and mechanical factors. He thinks that the initial lesion is a pigmented and purpuric angiodermatitis which is evidenced by three signs: pigmentation varying in degree and extension, lenticular purpura and more or less intense, parakeratotic, inflammatory changes close to the ulcer. That ulcers develop most frequently at the site of the branches of the internal saphenous vein is due to a mechanical circulatory factor and not to alterations in the saphenous vein. Ulcers of the leg appear following insignificant trauma or trifling infection because the "terrain" has been prepared by the dermatitis. Their treatment is discussed.

ERRONEOUS DIAGNOSIS OF CARCINOMA OF THE TONGUE. CARLOS ABAD, Prensa méd. mex. **60**:122 (Aug.) 1941.

The author reports a case of ulcerative tuberculosis of the tongue and pharynx which was believed to be a carcinoma because the first ulcer had developed on a plaque of leukoplakia. The clinical appearance was so typical of carcinoma that biopsy of a lymph node was performed only to determine the degree of malignancy of the tumor. The histologic picture was that of tuberculosis.

M. E. OBERMAYER, Los Angeles.

COURSE OF SYPHILIS IN PROSTITUTES. H. BUCHWALD, Arch. f. Dermat. u. Syph. **181**:385, 1940.

Of 300 prostitutes, 28 had chancres, 168 had secondary syphilis, 102 had latent syphilis and 2 had tertiary syphilis; 136 had no knowledge of infection.

Of 168 with secondary syphilis, 59 showed only papules in the genital region or in the mouth (infectious recurrent secondary syphilis).

Even after four years of infection, an extraordinarily high percentage (42.8 per cent) showed late recurrences. The number of recurrences was inversely proportional to the number of courses of treatment. The appearance of late syphilis and syphilis of the central nervous system was not influenced by previous treatment. Seven of 31 patients with secondary syphilis were clinically and serologically normal for a long time in spite of insufficient treatment. In 11 of 41 with latent syphilis the serologic reaction reverted to positive. Of 67 with latent syphilis 4 showed fixed positive reactions of the blood. Of 21 patients with latent syphilis the serologic reaction of 4 reverted to negative in spite of insufficient treatment. Of the patients with secondary syphilis 3.75 per cent had negative reactions of the blood.

Some patients without signs of syphilis suddenly had positive Wassermann reactions, which spontaneously reverted to negative.

LOCAL TREATMENT OF CHRONIC CUTANEOUS ULCERS WITH DIETHYLSTILBESTROL: VASCULAR EFFICACY OF SYNTHETIC ESTROGENS. D. WAGNER, Arch. f. Dermat. u. Syph. **181**:395, 1940.

In view of the efficacy of estrogenic substances in the treatment of disturbances of peripheral circulation in women at puberty, during pregnancy, at the menopause and during periods of hormonal dysfunction and considering the use of estrogens

in the treatment of acrocyanosis, Raynaud's disease, endarteritis obliterans, ulcus hypostaticum and gastrointestinal ulcers, the authors used diethylstilbestrol locally on various types of resistant ulcers associated with severe vascular change.

One to two ampules of an oily solution were applied locally daily and allowed to be absorbed. After epithelization had started an ointment was used.

Case 1: A youth aged 18 who had scleroderma with ulcers on the left leg and thigh improved.

Case 2: A patient with a trophic ulcer on the dorsum of the right foot with endarteritis obliterans, who had had sympathectomy without healing, showed slight improvement; then the condition became stationary.

Case 3: A man aged 64 with a roentgen ray ulcer on the left temple following treatment of basal cell carcinoma improved.

Case 4: In a woman aged 70, a roentgen ray ulcer on the right side of the forehead healed on application of ointment.

Case 5: A woman aged 77, with a roentgen ray ulcer on the left temple improved.

Case 6: A woman aged 57, with a roentgen ray ulcer following treatment of carcinoma of the scalp improved.

Case 7: A woman aged 44, with a roentgen ray ulcer following treatment of carcinoma in facial lupus vulgaris improved.

Case 8: A man aged 35, with a roentgen ray ulcer following treatment of carcinoma in a burn scar improved.

Case 9: In a man aged 70 carcinoma of the sole of the foot treated with roentgen rays with subsequent ulcer formation healed. Other treatment also was used.

The author attributes the beneficial effects in these cases to action on the blood vessels.

PHENYLARSENKERATINATE (ARSENODETOXIN) IN THE TREATMENT OF HUMAN SYPHILIS. D. WAGNER, Arch. f. Dermat. u. Syph. **181**:404, 1940.

Arsenodetoxin (a condensation product of a substituted aminooxyphenylarsenoxide with a higher molecular keratin hydrolysate) was given to 64 syphilitic patients, predominantly in the early stage of the disease. Clinically, serologically and parasitologically its effects compare favorably with those of the arsphenamines. Complications were mild: pains (1 patient), fever (1 patient) and nitritoid crisis followed by a morbilliform eruption with the second injection (3 patients).

Nine of 10 patients who could not tolerate arsphenamine received the arsenical keratinate without difficulty.

INFLUENCE OF TITRATION ALKALINITY OF CLEANSING AGENTS ON THE p_H OF HUMAN SKIN. L. PEUKERT, Arch. f. Dermat. u. Syph. **181**:417, 1940.

Unavoidable cleansing of the skin of workers with raw materials decreases the protective acidity of the skin and predisposes to the production of dermatitis. Ordinary cleansing solutions have a p_H of about 9 and influence the acidity of the skin to a degree which depends on the quality of the skin and not merely the actual alkalinity but the titration alkalinity or the buffer capacity, in which the ionic reserve plays a role.

The authors measured by the modified Bülmann hydroquinone glass electrode method the reaction of the cutaneous surface and the actual alkalinity and potential alkalinity (buffer capacity) of five cleansing solutions. Actual alkalinity varied from p_H 9 to 10, while the potential alkalinity varied from 6.5 to 50 (cubic centimeters of normal hydrochloric acid necessary to lower the p_H to 5.5).

A simplified practical method for determining relative buffer capacity is by use of phenolphthalein, which becomes colorless at about p_H 8.5. The normal p_H of the skin was determined and repeated at intervals after washing the skin with 1 Gm. of various cleaners for one minute. The p_H rose sharply and returned to normal or nearly normal in four hours.

The titration alkalinity of a cleanser with actual alkalinity over p_H 9 should not be over 10 (i. e., 10 cc. of normal hydrochloric acid should reduce the p_H of 100 cc. of a 10 per cent solution below p_H 8.5).

GASTROINTESTINAL CHANGES IN PEMPHIGUS. ST. V. PASTINSZKY, Arch. f. Dermat. u. Syph. **181**:451, 1940.

Necropsy revealed gastrointestinal ulcers in 5 of 22 patients with pemphigus. Two of the 5 had perforations into the peritoneal cavity. Gastrointestinal catarrh was diagnosed in 3 cases. These changes were specific (bullae, erosions, ulcers, scars or pigmentation) or nonspecific (gastritis, enterocolitis or hemorrhage). The great discomfort and weakened condition of each patient made complete examination and evaluation of clinical symptoms difficult; perforated ulcer was associated with signs and symptoms of peritonitis.

Analysis of gastric contents of some patients showed 40 per cent to have normal, 25 per cent decreased and 35 per cent increased gastric acidity. Eosinophilic leukocytes were found in 60 per cent of the cases; hemosiderin-containing cells appeared in 20 per cent of the cases, signifying hemorrhage. The author believes that pemphigus may involve the gastrointestinal tract in pemphigus vulgaris and pemphigus foliaceus but rarely in pemphigus vegetans. BECKER, Chicago.

CASES OF ATYPICAL SUPERFICIAL EPITHELIOMATOSIS. H. G. PIPER, Dermat. Wchnschr. **112**:429 (May 31) 1941.

Multicentric epitheliomas of the trunk are known to be relatively benign; they remain unchanged through life, without giving rise to metastases. Formation of ulcers or tumors occurs only with exceptional rarity. The author reports 3 cases of such exceptions which came under his observation within a few months. In 2 cases flat epitheliomas of the skin formed nodules, which later developed into fungating tumors. Histologically one of the tumors had remained a basal cell epithelioma, while the other began to show transition toward squamous cell epithelioma. The third case showed carcinomatous ulcerations of the back and also multicentric epitheliomas of the trunk and psoriasis. Histologically these ulcerations were basal cell epitheliomas. The author mentions the not infrequent combination of psoriasis and epithelioma of the skin and also a rare case of parapsoriasis en plaques with multicentric epitheliomas of the trunk.

ETIOLOGY OF REITER'S DISEASE (CONJUNCTIVAL-URETHRAL-SYNOVIAL SYNDROME). KRUSPE, Dermat. Wchnschr. **112**:457 (June 7) 1941.

Most authors associate Reiter's syndrome of conjunctivitis, urethritis, arthritis and hyperkeratoses with gonorrhea. In dermatologic literature this syndrome is usually called gonorrheal hyperkeratoses (Vidal-Jacquet). The author cites Kuske (*Arch. f. Dermat. u. Syph.* **179**:58, 1939), who pointed to the intestinal tract or to the urogenital system as possible points of entry for an infection with Bacillus coli or other organisms. Kuske also mentioned the fact that gonococci have been shown to be present within the cutaneous lesions only in a few isolated instances and then only by direct staining methods, never by culture. The author observed Reiter's syndrome in 7 German soldiers stationed in the Bretagne in France. They were suffering from bacillary dysentery, which the author considers as the cause of Reiter's disease. WILLIAM CURTH, New York.

TUMORS ON THE LOWER EXTREMITIES AND MALIGNANT CHANGES IN ULCERS OF THE LEG; CYLINDROMA IN A CASE OF ULCUS CRURIS. K. HÜBSCHMANN and V. JEDLIČKA, Acta dermat.-venereol. **21**:239 (March) 1940.

The authors describe a case of a typical varicose ulcer in which the development of a growth was noticed. The histologic examination showed the presence of cylindroma. The authors believe that the malignant degeneration was due to chronic irritation by the ulceration. It is possible that the continued cauterization with silver nitrate (for one year) was a contributory factor.

CUTANEOUS MANIFESTATIONS OF LYMPHOGRANULOMATOSIS BENIGNA SCHAUMANN. E. B. VOSBEIN and PAUL BONNEVIE, Acta dermat.-venereol. **21**:408 (March) 1940.

The authors discuss the clinical, morphologic and histologic features of 34 cases of generalized sarcoidosis. Sixteen patients presented cutaneous lesions characteristic of Boeck's sarcoid. The nodular lesions were small, reddish, solid and slightly prominent. The nodose lesions were coin-sized, bluish red, rather solid plaques which presented a varying number of superficial dilated blood vessels. There were nontypical forms in 18 cases. Lupus-vulgaris-like lesions were present in 7 cases. Three patients presented angiolupoid. Annular forms localized on the face were observed in 3 cases. One case each of eruptions resembling psoriasis, lupus erythematosus and erythema nodosum were also observed. Roentgen observations on the lungs and bones are cited.

The main factors in making the diagnosis of Schaumann's disease, particularly in the nontypical cases, are discussed. The methods and results of treatments are cited.

ASTRACHAN, New York.

Society Transactions

METROPOLITAN DERMATOLOGICAL SOCIETY

THOMAS N. GRAHAM, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

New York, March 17, 1941

A Case for Diagnosis (Dermatitis Venenata? Psoriasis?). Presented by DR. HENRY D. NILES.

F. B., a white woman, was first seen by me in February 1941. She stated that some lesions appeared on her left palm and middle finger and on the dorsum of her left hand seven months ago. These spread to the left forearm and arm and two months ago to under the left breast, and one week ago a spot appeared on the inner side of her left leg. There have been no lesions on the right side of her body. The lesions at first looked like lichen planus and later like guttate psoriasis, and those on the fingers were followed by ridging of the nails. She went without nail polish for one week, without benefit. For years she has sat with her left arm resting on the arm of a henna-colored armchair. The rash first appeared while she was on her summer vacation but was much better while she was on Christmas vacation.

Examination reveals a few pinhead-sized scaly lesions resembling dried vesicles on the left palm, several flat, slightly raised, warty lesions containing pinpoint-sized keratotic plugs on the dorsa of the left hand and fingers and some similar lesions, as well as streaks and patches of eczematous erythema and scaling, on the flexor surfaces of the left arm and forearm. There are some fainter eczematous patches under the left breast and one small spot on the inner side of the left leg. There are no lesions on her scalp, face or neck or on the right side of her body. She has had six or eight roentgen ray treatments, the last one about a month ago, which cleared up some of the old lesions, but new ones appear. Microscopic diagnosis of a specimen from the arm was dermatitis. Examination showed no evidence of tinea.

DISCUSSION

DR. LAIRD S. VAN DYCK: I should call the condition a linear lichenoid dermatitis, after ruling out linear lichen planus, psioriasis and linear nevus. Since the histologic diagnosis is dermatitis and in view of the clinical picture, I think that diagnosis can be accepted.

DR. RICHARD J. KELLY: My first impression was that the lesion looked like parapsoriasis clinically. I did not get a full history; it is difficult to accept this eruption as dermatitis venenata because of the distribution.

DR. MAURICE J. COSTELLO: The best diagnosis I can suggest is linear lichenoid dermatitis with zosteriform distribution. I do not think that the condition is dermatitis venenata. I should expect this eruption to respond to the administration of fractional doses of roentgen rays or of mercury salicylarsenate.

DR. FRANKLIN H. GRAUER: I think the diagnosis in this case probably is dermatitis venenata or contact dermatitis. It is possible, of course, that a dermatitis such as this might resemble psoriasis microscopically, because after all there are psoriasiform eczemas. As a result of rubbing it might become lichenified and superficially even resemble lichen planus. I do not know what causes it.

DR. HENRY D. NILES: The patient has been under expert dermatologic care since December. I still think that dermatitis venenata is the probable diagnosis. I found that she frequently sits in a chair with her left arm resting on the arm of the chair and with a book in her right hand. She has no eruption on her right arm, perhaps because this does not come in contact with the chair. She has had the article of furniture for a long time, and it is conceivable that it might be the cause of her dermatitis. Psoriasis can be ruled out because of the histologic picture, which showed no suggestion of anything but dermatitis. The case is puzzling. It resembles the cases of lichen striatus recently described by Senear and Caro (Senear, F. E., and Caro, M. R.: Lichen Striatus, ARCH. DERMAT. & SYPH. **43**:116 [Jan.] 1941).

Lupus Vulgaris Erythematodes (Leloir). Presented by DR. FRANKLIN H. GRAUER.

M. H., a white woman aged 51, born in the United States, first had the present eruption about forty years ago, when she was 11 years old. Since that time it has gradually spread to its present size. There have been no symptoms except that during the cold weather when the eruption becomes dry and scaly, it is apt to burn and smart. There is no history of tuberculosis. On the right side of the chin there is a sharply defined, slightly elevated, brownish red patch the size of a silver dollar. Its surface is somewhat scaly; there are some telangiectases, and on diascopic pressure the lesion is seen to be composed of numerous, glass pinhead–sized apple jelly nodules. The Wassermann reaction of the blood was negative. A biopsy revealed groups of histiocytes surrounded by small round cells distributed throughout the middle and upper parts of the cutis. The vessels were not congested. The epidermis was thin, and the rete pegs were flattened. A microscopic diagnosis of lupus vulgaris was made. Treatment to date has consisted of a low sodium chloride, high vitamin diet and generalized exposures of ultraviolet radiation. The patient is presented for therapeutic suggestions.

DISCUSSION

DR. LAIRD S. VAN DYCK: As regards therapy in this case, I should prefer surgical excision and a full thickness graft.

DR. RICHARD J. KELLY: I agree with the diagnosis, but I am not sure that a full thickness graft would be the best measure. If an endotherm excision were made, the scar would be unsightly. I do not recommend roentgen ray therapy.

DR. MAURICE J. COSTELLO: Since the patient has had the eruption for years, I think that some lotion or tinted cream might make it less conspicuous. It is not disfiguring even at present. If I decided to treat this lesion, I should partition it and destroy it in several stages by cautery or electrodesiccation. I have treated several patients with lupus vulgaris of the face by this method, with good therapeutic and cosmetic results. Early recurrences are easily managed.

DR. HENRY D. NILES: I agree with Dr. Costello. I have had 3 or 4 patients with lupus vulgaris whom I treated with electrocoagulation and curettage. There are likely to be some recurrences, but these can be treated again. The treatment is given with the patient under procaine hydrochloride anesthesia; it is painless, and the results are good. I have seen several middle-aged women with lesions of lupus vulgaris in this area and under and along the sides of the jaw, but according to the textbooks these are not considered areas of predilection. In these areas the scar is not so conspicuous because it is partly shaded by the jaw.

DR. THOMAS N. GRAHAM: It is not infrequent for lupus vulgaris with no other evidence of tuberculosis to terminate in pulmonary tuberculosis. Having observed several such cases, I believe that, in spite of the long duration of this patient's eruption and its apparent inactivity, it would be much safer to destroy the lesions than to cover them up.

DR. FRANKLIN H. GRAUER: This patient originally came to me to be sure that the lesion was not cancer of the skin. She is apprehensive, and unless one can be certain that the therapeutic result will be less conspicuous than the present lesion, she prefers not to have anything done. Because of her apprehension, her age and the fact that the lesion has not increased much in size during the past twenty years, I finally decided that it might be better not to destroy the lesion but to keep the lesion under observation and to have the patient cover it with cosmetics.

Dermatophytosis and Tinea Glabrosa (Caused by Trichophyton Purpureum). Presented by DR. ROYAL M. MONTGOMERY.

O. D., a Cuban woman aged 25, married, has had the present eruption for the past eight months on the feet, for three months on the hand and for one month on the thigh. There are scaling and maceration between the toes of the left foot and a sharply marginated erythematous excoriated patch on the left sole extending onto the instep. On the plantar surfaces of the toes the skin is dull red and there is a fine branny scaling. The right foot is apparently normal. The big toe nail of the left foot is slightly undermined and yellow. On the dorsum of the left hand there is an eczematous eruption which extends onto the fingers. The left palm is indurated, dry and covered with a fine scale. The left fourth finger nail is undermined, and the distal half is broken off. The right hand is normal. There is a palm-sized, circinate, lichenified patch on the inner surface of the left thigh. A small eczematous patch is present on the extensor side of the left knee. The Wassermann reaction of the blood was negative. Examination of the left sole, toes, toe nail, thigh, hand and finger nail showed evidence of tinea. Trichophyton purpureum was cultured from the hand, finger nail and thigh.

DISCUSSION

DR. LAIRD S. VAN DYCK: I agree with the diagnosis. I think it is a good plan to show as many cases of this type as possible in order that dermatologists may be constantly aware of the increasing prevalence of infections of the skin and nails with T. purpureum, some of which fail to heal after years of diligent and careful treatment by experts.

DR. RICHARD J. KELLY: I was much interested in seeing a condition as extensive as this is. I should like to know if Dr. Montgomery has confirmed the cultural observations.

DR. MAURICE J. COSTELLO: Since it is true that patients with this condition are hyposensitive to trichophytin, is there any way of increasing the sensitivity and changing the torpid inflammatory reaction to a more active one?

DR. HENRY D. NILES: I think this case is most instructive as well as interesting. Some one mentioned that the lesions on the thigh resemble neurodermatitis but are annular. An interesting feature is that only one hand is involved. That hand is dry, but the other palm shows hyperhidrosis. Only one foot and one finger nail are involved.

DR. ROYAL M. MONTGOMERY: I think the case is interesting because the lesions on the thigh simulate those of neurodermatitis and also because the extensive eruption on the hand simulates a common contact dermatitis. The point that leads one to a diagnosis of tinea is the suggestive appearance of the finger nail on the left hand.

A Case for Diagnosis (Chronic Purpuric Lichenoid Dermatitis of Gougerot and Blum?). Presented by DR. HENRY D. NILES.

L. M., a white woman aged 52, born in Hungary, was first seen in the dermatologic clinic of the New York Hospital on March 17, 1941. She had an eruption on her knees, legs and extensor surfaces of the forearms of two years' duration.

This consisted of many pinpoint-sized, red to brown purpuric spots and small slightly thickened scaly lichenified patches. There were five or six pinpoint-sized purpuric spots on the mucosa of the left cheek. She said that she had frequent epistaxis and bleeding of the gums. There was a question whether she had had adequate intake of vitamin C. The lesions were limited to her extremities.

DISCUSSION

DR. ROYAL M. MONTGOMERY: The lesions are certainly all purpuric. I was wondering if she had vitamin C deficiency. I did not inquire as to her diet. There is a simple test to determine capillary fragility. First determine the systolic and diastolic blood pressure. Then pump up the sphygmomanometer to a point midway between systolic and diastolic pressure and allow it to remain there for ten to fifteen minutes. The number of petechiae are counted in two circles, 2.5 cm. in diameter, the centers of which are 4 cm. below the crease on the flexure side of the elbow. The average is taken. Up to 10 petachiae are normal; above 20 petechiae means definite capillary fragility. It would be interesting to see the results of this test in this patient.

DR. FRANKLIN H. GRAUER: An eruption like this suggests several diagnostic possibilities, i. e., Schamberg's progressive pigmentary disease, purpura annularis telangiectodes (Majocchi's disease), angioma serpiginosum, chronic purpuric lichenoid dermatitis and hereditary familial telangiectasia (Rendu-Osler). Taking into consideration all the characteristics of this patient's eruption, namely its extensive distribution, the fact that the lesions are actually purpuric, the absence of annular lesions and the presence of lichenoid papules, I think the most likely diagnosis is that suggested by the presenter, chronic purpuric lichenoid dermatitis. One question I should like to ask is whether any one has ever seen lesions of the mucous membranes in this condition.

DR. LAIRD S. VAN DYCK: I agree with the diagnosis of chronic purpuric lichenoid dermatitis of Gougerot and Blum.

DR. RICHARD J. KELLY: I think these lesions fit in with that description rather than with that of Osler's disease. The patient did not have any lesions on the face that resembled strictly the hemangioma type of Osler's lesions. She did have a few on the mucous membranes and around the gums and buccal mucosa that could be taken for small hemangiomas.

DR. MAURICE J. COSTELLO: I have seen only 1 patient suffering from this dermatitis whose clinical features satisfied me in all respects. I suggest a blood platelet count and a snake venom test for this patient.

DR. HENRY D. NILES: I suggested the diagnosis given for the reasons that Dr. Grauer covered. The patient certainly has papular lichenoid lesions and slight scaling. I do not remember whether lesions on the mucous membranes and arms have been described with this condition; as I recall it has been reported only on the legs.

Ainhum. Presented by DR. ROYAL M. MONTGOMERY.

S. M., a Negress aged 48, single, has had the present condition for four years. She was born in Roanoke, Va., and has been in New York city for forty years. Her father and mother and grandparents were born in Virginia. The patient states that some one stepped on the now affected toe nine years ago. At present there is a deep constricted band on the proximal end of the fifth right toe. This constriction encircles the toe and is present on the dorsum. The plantar side of this constriction is macerated. Previous to using paste of zinc oxide N. F. she complained of pain. At present there is none. The Wassermann reaction of the blood was negative. A roentgenogram of the affected toe showed constriction of the soft tissue but no definite bony changes.

Ainhum. Presented by DR. ROYAL M. MONTGOMERY.

M. C., a man aged 36, a teacher, has had the present condition for two years on the left small toe and for one and one-half years on the right small toe. He is married and has two children. He was born in Savannah, Ga., and has been in New York city for the past twenty-two years. His mother and father were born in Savannah, Ga., and his grandparents were born on an island off the coast of Georgia. No one in his immediate family nor any of his relatives have this disease. The left fifth toe is constricted proximal to the toe nail. The constriction encircles the toe, being more constricted on the under surface. The distal portion is slightly swollen. The right fifth toe is also constricted. This constriction is greater on the under surface of the toe just proximal to the toe nail. The Wassermann reaction of the blood was negative. A roentgenogram of each affected toe showed a constriction of the soft tissue at the base of the middle phalanx. There were no definite bony changes in any of the phalanges. Previous to using paste of zinc oxide there were painful fissures on the plantar side of the constrictions. At present these fissures are healed, but the area is hyperkeratotic and macerated.

DISCUSSION OF TWO CASES OF AINHUM

DR. LAIRD S. VAN DYCK: I think ainhum should be taken out of the category of tropical diseases. Its occurrence has been reported in several native-born Americans who have never been outside of the United States.

DR. MAURICE J. COSTELLO: I have seen this clinical entity only in Negroes. The most baffling question is that of causation: Is it a neurologic disturbance, i. e., trophic in origin? The roentgenograms showed definite osseous changes in the bones of the affected small toes.

DR. ROYAL M. MONTGOMERY: Hòrowitz and Tunick (ARCH. DERMAT. & SYPH. **36**:1058 [Nov.] 1937) and R. L. Sutton Jr. (ARCH. DERMAT. & SYPH. **38**:26 [Jan.] 1938) have recently reported cases of ainhum. They suggest various causes, such as chronic irritation, leprosy, bandlike sclerodermas, sclerodactylia and Raynaud's disease. Thus there is no definite causation. There have been a number of cases reported in Negroes in the southern and eastern coast states. Ainhum has also been reported in the white race. Sutton's case was that of a white boy, and the condition was reported as "ainhum-like hyperkeratosis."

Arsenical Pigmentation and Keratoses Superimposed on Dermatitis Herpetiformis. Presented by DR. LAIRD S. VAN DYCK.

E. G., a man aged 34, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 10, 1941, with a generalized eruption of four years' duration. The eruption began on the right buttock with blisters which broke, crusted and healed, leaving pigmented spots. Three years ago the patient began taking solution of potassium arsenite U. S. P., 3 to 10 drops three times a day. About a year after he began taking arsenic he noticed warty lesions beginning to appear on the hands. He has continued to take the arsenic solution at intervals up to the present because he has found that to be the only medication which gives him relief from the intense itching. At present the skin of the entire body is irregularly pigmented with small spotty areas and there is clear skin between the pigmented spots. There are also many scattered, somewhat grouped excoriated lesions. The skin is dry and in some places shows a fine scaling. There are hyperkeratosis and numerous warty lesions on the palms and soles with a few discrete punctate keratoses of the dorsal aspect of the fingers. The nails are thickened, lamellated and brittle. The Wassermann and Kahn reactions of the blood were negative. The urine was normal. A blood test for arsenic was negative. The carbon dioxide–combining power of the blood was normal. Biopsy of tissue from a lesion taken from the dorsum of the hand revealed keratosis, and of tissue from the left arm, inflammatory reaction.

DISCUSSION

DR. RICHARD J. KELLY: There is no doubt that this patient has superimposed pigmentation from arsenic. The underlying condition looks like dermatitis herpetiformis.

DR. MAURICE J. COSTELLO: It is unusual for solution of potassium arsenite U. S. P. in the doses self administered to produce such extensive, serious changes in the skin in a relatively short time. It is possible that the patient's occupation as a painter brings him in contact with lead. The synergistic action of these drugs, lead and arsenic, may increase the rapidity of absorption and decrease the rate of elimination.

DR. HENRY D. NILES: I agree with Dr. Costello that the patient's severe and rapid eruption may have been caused by the exposure to lead. I suggest making a lead determination and examining a blood smear for stippling. The gums should be examined for a lead line.

DR. ROYAL M. MONTGOMERY: The thing that interests me most was that the keratoses are thicker on the palm than on the soles. In most of the cases I have encountered the keratoses seemed more severe on the feet.

DR. THOMAS N. GRAHAM: My impression of the palmar keratosis in this case is that it is an unusual type of arsenical hyperkeratosis. In most of the cases which I recall having observed there has been a generalized palmar hyperkeratosis with fissuring, and not discrete patches as observed in Dr. Van Dyck's case.

DR. LAIRD S. VAN DYCK: The common type of arsenical keratosis is a discrete punctate lesion resembling a hard wart. This patient's lesions are so numerous and so close together on the palms as to give the appearance of a solid mass of horny material. An examination for lead has not been made.

Amyloidosis Cutis. Presented by DR. THOMAS N. GRAHAM.

R. L., a white man aged 48, born in Puerto Rico, was first seen in the Knickerbocker Hospital on Feb. 25, 1941. He presented an eruption of one year's duration, limited to the legs. Examination revealed numerous, indurated, discrete and grouped, grayish, slightly erythematous, translucent-appearing papules ranging in diameter from 0.2 to 0.5 cm. on the extensor, medial and lateral aspects of the legs. The patient complained of considerable pruritus. The Wassermann and Kahn reactions of the blood were negative. The urine was normal. The blood sugar content was 99 mg. per hundred cubic centimeters. A blood count showed 4,750,000 erythrocytes and 14,000 leukocytes, with 87 per cent polymorphonuclear leukocytes, of which 81 per cent were polymorphonuclear neutrophils, 6 per cent eosinophils and 13 per cent lymphocytes. The subcutaneous injection on February 27 of a 1 per cent sterile solution of congo red at the site of a group of the lesions resulted in a retention by the papules of the dye, producing a rose-red color which persisted for three weeks.

Microscopic examination of a biopsy specimen showed islands of amyloid generally scattered throughout the upper part of the corium. This observation was confirmed by a methyl violet stain.

DISCUSSION

DR. LAIRD S. VAN DYCK: I agree with the diagnosis. This is the best demonstration I have seen of the effect of the injection of congo red into the lesions of amyloidosis cutis.

DR. HENRY D. NILES: I should be interested to learn whether roentgen ray therapy would help these lesions. Some authors have reported at least partial improvement, but none of the patients with amyloidosis whom I have treated with roentgen rays have shown improvement.

DR. ROYAL M. MONTGOMERY: In reference to roentgen ray therapy, conditions of this type have been diagnosed as lichen planus and much roentgen ray therapy has been given without success. Later they were proved to be amyloidosis.

DR. FRANKLIN H. GRAUER: This eruption is a typical example of this condition. I do not think anything will benefit these patients very much. As Dr. Niles suggests, roentgen rays may at times be of help, providing the condition is not of too long standing. When lichen amyloidosis was first described I was struck by at least the superficial similarity of this eruption to photographs I had seen of lichen planus ocreaformis (Lieberthal). I understand, however, that this question was raised at a meeting of the Chicago Dermatological Society and that the consensus among the members who had observed the original case of lichen planus ocreaformis was that the two conditions are not the same.

DR. THOMAS N. GRAHAM: I shall try roentgen ray therapy and the administration of arsenic, as has been suggested. Treatment to date has consisted only in antipruritic lotions. I shall also make a Benhold test, injecting 10 cc. of a 1 per cent sterile solution of congo red intravenously, to determine whether the patient has generalized amyloidosis. Retention of more than 30 per cent of the dye after one hour is suggestive of generalized amyloidosis. This test is used frequently by internists and is not considered to be dangerous.

NOTE.—The Benhold test, subsequently performed, showed no abnormal retention of the dye, indicating that the patient did not have generalized amyloidosis.

Dermatomyositis, Diffuse and Generalized. Presented by DR. MAURICE J. COSTELLO.

M. S., a woman aged 29, was first seen by me in December 1940. Her skin was diffusely hidebound, glazed, thickened and slightly scaly. The areas of severe involvement were the supraclavicular and infraclavicular regions, arms, forearms, wrists, hands, fingers, posterior portions of the thighs and ankles. She also complained of difficulty in swallowing. The patient stated that this condition had started about five weeks before. There were areas of hyperpigmentation and depigmentation, and there were limitation of the motion of the wrist and finger joints, stiffness of the vertebral column and a thinning tapering hardness and hidebound condition of the skin of the fingers. She had fatigue, anorexia, arthritic pains and loss of weight. The calcium content of the blood was 9.2 mg. per hundred cubic centimeters. The following results of laboratory tests were obtained at the Vanderbilt Clinic in December 1940: The urine was normal. The reaction to a Kline test was negative. The basal metabolic rate was + 21 per cent. The hemoglobin content of the blood was 81 per cent. The erythrocyte count was 4,330,000 and the leukocyte count 11,100. A differential count showed polymorphonuclear leukocytes 63 per cent, small lymphocytes 30 per cent, large lymphocytes 2 per cent and eosinophils 5 per cent. The results of chemical examination of the blood were as follows: serum phosphatase, 3.5 Bodansky units; inorganic phosphorus, 3.7 mg.; protein, 7.2 Gm. (albumin 4.6 Gm.), and nonprotein nitrogen, 28 mg. per hundred cubic centimeters. The reaction to a cephalin flocculation test was negative. Treatment consisted of ultraviolet irradiation and the administration daily of adrenal cortex extract (cortate) 1 cc., liver extract 2 cc., estradiol benzoate 2,000 international estrogen units and recently a 0.5 per cent solution of dihydrotachysterol in oil (5 mg. in 1 cc.) 2 cc. She is also taking capsules of vitamin B complex and drisdol (crystalline vitamin D_2) in propylene glycol 15 drops daily. Her body is massaged for one hour daily.

DISCUSSION

DR. HENRY D. NILES: I agree with the diagnosis. The condition in this case is extensive.

DR. FRANKLIN H. GRAUER: I should try injections of dihydrotachysterol with the patient under hospital observation and adequate laboratory control.

DR. LAIRD S. VAN DYCK: Some of the French school of dermatologists believe that scleroderma is due to hyperparathyroidism, with an increased mobilization of ionized calcium in the blood and its subsequent deposition in the skin. Para-

thyroidectomy has been advocated for that reason. If I am not mistaken, dihydrotachysterol acts like parathyroid extract in mobilizing calcium from the bones and increasing its concentration in the blood. Is not that the very thing that one should aim to avoid in cases of scleroderma?

DR. MAURICE J. COSTELLO: The interesting feature of this patient's eruption is that the extensive changes have occurred since November 1940.

NOTE.—The patient died in September 1941.

THOMAS N. GRAHAM, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

New York, April 21, 1941

Sycosis Vulgaris and Ulerythema Ophryogenes. Presented by DR. HENRY D. NILES.

V. B., a man aged 30, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of an eruption of two and one-half years' duration.

The eruption first appeared on the left eyebrow. Later a large furuncle developed on the right cheek, which was brought to a head with the application of a salve and opened spontaneously. Subsequently the eruption involved the entire face, but there was little pruritus. A febrile disease at the age of 19 caused alopecia in the pubic area.

Examination revealed erythema, atrophy and alopecia of the left eyebrow and a palm-sized similar patch on the left temple. There were crusted lesions and erythema on the anterior surface of the right ear lo[illegible], and the face and neck showed faint remains of the eruption. On the nape of the neck were two or three crusted deep pustules, and the patient had some blepharitis.

The patient has had 2 skin units of roentgen radiation to his face. He stated that the hair fell from his left eyebrow and temple after the roentgen ray treatments. For the past week he has been using sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) locally, 20 per cent in glycerin, and has taken sulfathiazole orally, 0.5 Gm. four times daily for five days. He has shown considerable improvement.

The results of a complete blood count and urinalysis were normal. The Wassermann reaction of the blood and the Kahn reaction were negative.

DISCUSSION

DR. LESLIE P. BARKER: This patient had definite roentgen ray changes on the face, especially on the cheeks and chin, and the eruption elsewhere, I think, would fit into the picture of lupoid sycosis.

DR. LAIRD S. VAN DYCK: Loss of hair in the pubic region due to an acute illness accompanied by high fever is undoubtedly rare.

DR. HENRY D. NILES: I presented this patient partly to have some discussion as to whether the alopecia was due to the disease or to the radiation. It is a difficult question to answer. According to the note which I obtained from Dr. Andrews, he gave the patient at the most a total of 1½ skin units in doses of ¼ skin unit. The patient was given ½ skin unit at the hospital, thus receiving a total of 2 skin units. It is hard to believe that such a small amount of radiation could cause alopecia. Alopecia in the pubic area is unusual. The patient stated that he had no alopecia elsewhere. I believe it to be a permanent alopecia areata without relation to the condition of the face.

Dermatitis Herpetiformis: Results of Treatment with Sulfathiazole. Presented by DR. LAIRD S. VAN DYCK.

S. E., a man aged 20, a student, was first seen on March 11, 1941 with an eruption of three months' duration on the scalp, in the nuchal region, axillas and cubital and popliteal spaces and on the elbows, buttocks and knees. One year previous to the onset he sustained a skull fracture in the left temporal region and floor of the orbit, but otherwise he has always been perfectly healthy.

The eruption consisted of grouped vesicular and bullous lesions with a herpetic appearance, symmetrically distributed over the areas previously mentioned. There was slight reddish brown pigmentation in some of the areas but no definite scarring. Itching has been severe.

For three weeks attempts were made to relieve the itching with local treatment, without success. He was then given sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) in doses of 15 grains (1 Gm.) four times a day for two days, followed by 0.5 Gm. four times a day. Itching was relieved within thirty-six hours after he was given the sulfathiazole. Two weeks later the eruption had almost completely disappeared except for pigmentation. Medication was discontinued four days ago. Since the administration of sulfathiazole was stopped a few new vesicles have appeared on the face and elbows.

DISCUSSION

DR. ANTHONY C. CIPOLLARO: I think the result is remarkable. Since Dr. Costello presented the first case in which there was improvement with this treatment, I have had 2 cases in private practice in which there has been improvement. Unfortunately in both cases the disease recurred and I did not feel justified in continuing treatment with sulfathiazole.

DR. HENRY D. NILES: The feature that interests me most in this case was the presence of lesions on the face, which I have rarely, if ever, seen before in dermatitis herpetiformis. I have seen them on the scalp but not on the face.

DR. LESLIE P. BARKER: I often wonder if one is justified in giving sulfathiazole for such a long time. Certainly its administration cannot be continued throughout the life of the patient, and each time the therapy is discontinued dermatitis herpetiformis recurs.

DR. MAURICE J. COSTELLO: I was interested to note that the clinical improvement in the patient presented by Dr. Van Dyck was similar to that in one presented by me at a meeting of the Manhattan Dermatologic Society (ARCH. DERMAT. & SYPH. **41**:134 [Jan.] 1940). My patient had relief of itching within forty-eight hours after sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) was administered. At the end of a week a severe, extensive, vesiculobullous form of dermatitis herpetiformis had completely disappeared, even though it had been present for five years. She has had no recurrence. Sulfanilamide and its derivatives are tolerated better by patients who are not suffering from diseases accompanied by severe constitutional reaction and fever. Patients with chancroids and lymphogranuloma venereum treated in the dermatologic wards at Bellevue Hospital have had few reactions, even though large doses are administered daily for six weeks.

DR. ROYAL M. MONTGOMERY: I have had a similar experience with sulfapyridine. A patient took sulfapyridine for three weeks, 21 grains (1.36 Gm.) a day. The eruption cleared in ten days. She has now been taking 7 grains (0.45 Gm.) a day for five months. Her blood picture is normal. She has been practically free from the eruption for this period.

DR. THOMAS N. GRAHAM: The result of treatment in this case is excellent. I wonder if a diagnosis of erythema multiforme can be definitely ruled out. This disease, too, has been reported as responding favorably to sulfanilamide therapy. The case presented is not a typical instance of dermatitis herpetiformis and has a number of features which suggest erythema multiforme bullosum. Absence of pigmentation is unusual in dermatitis herpetiformis.

DR. LAIRD S. VAN DYCK: I think the distribution and extent of the lesions are against erythema multiforme and especially the presence of herpetic vesicles. This patient has all the features of Duhring's disease except scarring. I expect to reduce the dose of sulfathiazole gradually and try to find a maintenance dose. He has had a blood count and urinalysis every week. There has been no depression in the leukocyte count, and the urine is normal. I think it is safe to continue giving the drug for a few weeks more and then gradually reduce the dose.

A Case for Diagnosis (Rosacea-Like Tuberculid of Lewandowsky or Acnitis). Presented by DR. MAURICE J. COSTELLO.

F. R., a woman aged 27, has had this eruption for one year. It is present on the cheeks, sides of the chin and forehead. It consists of numerous pinhead-sized, discrete, inflammatory, sago-grain-like papulopustules, from which can be expressed a small amount of seropurulent material. The individual lesion lasts about six weeks and is followed by a small superficial depressed cicatrix. No comedos are present. The papules increase in size as they reach the point of the chin.

A tuberculin patch test elicited a 4 plus folliculopustular eczematous solid reaction after forty-eight hours. There was a vesicular reaction to an intradermal test with a 1:100,000 solution of tuberculin. There is no personal or family history of tuberculosis, although the patient's fiancé has pulmonary tuberculosis with a positive reaction for tubercle bacilli in the sputum. A roentgenogram of her chest was normal.

This eruption has been refractory to all therapy administered thus far, which has consisted of twelve fractionated doses of superficial roentgen rays (75 r) to three areas of the face at weekly intervals. Eighteen injections of gold sodium thiosulfate, 25 mg., at two week intervals, dilute hydrochloric acid, 10 minims (0.6 cc.) three times a day, lotions, salves, diet and generalized ultraviolet irradiation were included in the therapy.

DISCUSSION

DR. LAIRD S. VAN DYCK: I agree with the diagnosis of rosacea-like tuberculid. My experience in treating this condition with injections of gold sodium thiosulfate has been disappointing. I believe tuberculin is a better therapeutc agent for this disease.

DR. ANTHONY C. CIPOLLARO: I agree with the diagnosis of rosacea-like tuberculid. I have encountered cases in which the condition responded to gold therapy, to tuberculin and sometimes even to strong doses of ultraviolet rays.

DR. HENRY D. NILES: I have had the same experience as Dr. Cipollaro. In most of my cases the condition has responded to a few injections of gold sodium thiosulfate, certainly much better than lupus erythematosus does. Several patients have responded to ordinary treatment of rosacea: white lotion N. F. and mild doses of ultraviolet radiation. I must admit, however, that in some cases the diagnosis was made only after the usual treatment for rosacea was ineffective. I then made tuberculin tests and a biopsy, and the conditions usually responded to gold therapy.

DR. LESLIE P. BARKER: Patients with this condition rarely respond to local treatment with white lotion N. F. and are usually sent to the dermatologist because they do not respond to the standard treatment for acne rosacea. Patients with this type of rosacea-like tuberculid of Lewandowsky have responded especially well to injections of tuberculin.

DR. THOMAS N. GRAHAM: I recall 2 cases in which the condition responded to intravenous injections of gold sodium thiosulfate after white lotion N. F. had been employed without benefit. The diagnosis in each case had been established by histologic study. Ten or twelve injections effected a cure.

DR. MAURICE J. COSTELLO: In spite of the various treatments this patient has received, the eruption has not improved. She has not received tuberculin therapy.

Arsenical Keratoses. Bowen's Precancerous Dermatosis? Presented by Dr. Royal M. Montgomery.

B. W., a white woman aged 42, has had the present eruption for ten years. On the soles there is a punctate hyperkeratosis. On several fingers there are small keratoses. There are also dry erythematous, scaly patches on the dorsum of the right foot, left knee and left thigh. There are smaller scaly macules on the dorsum of the left hand and about the wrists. There is a beginning leukoplakia on the right buccal mucosa. There is a history of the patient taking arsenical preparations for acne thirty years ago.

DISCUSSION

Dr. Laird S. Van Dyck: I agree with the diagnosis of both arsenical keratoses and Bowen's disease. I think it is extremely interesting to see both manifestations in the same patient coinciding with a history of arsenic ingestion many years previously.

Dr. Anthony C. Cipollaro: This case is so unusual that it should be written up. The red scaly patches resemble lesions of Bowen's disease. To be certain of the diagnosis one must perform a biopsy.

Dr. Henry D. Niles: I think this case is most interesting and instructive. It is well to keep it in mind in other cases in which one sees lesions of Bowen's disease without typical arsenical keratoses. I have seen many patients with psoriasis who have taken solution of potassium arsenite U. S. P. for years in whom basal cell epithelioma as well as keratoses develop.

Dr. Leslie P. Barker: I believe most patients who have multiple lesions of Bowen's disease or multiple superficial basal cell epitheliomas have a high arsenic content in the blood. Many of them have taken solution of potassium arsenite U. S. P. for a long time, and I think this has a definite etiologic bearing on this type of lesion.

Dr. Maurice J. Costello: I agree with the diagnosis. I think that all prescriptions containing arsenic, especially in the form of solution of potassium arsenite U. S. P., should be labeled clearly "do not repeat." The number of patients seen at several meetings of dermatologic societies presenting serious eruptions similar to that in the case in question are all too frequent.

Dr. Royal M. Montgomery: This patient also has a beginning leukoplakia on the buccal mucosa. Her dentist said it was from a draining sinus. At first a diagnosis of psoriasis was made because of the scaly appearance of the lesions.

Note.—A biopsy of tissue from a lesion on the left thigh on June 10, 1941 showed Bowen's disease.

A Case for Diagnosis (Sarcoid? Tuberculosis Cutis?). Presented by Dr. Leslie P. Barker.

M. H., a white woman aged 40, was first seen on May 10, 1937 with an eruption on both cheeks of ten months' duration. The lesions began as small red areas symmetrically placed on the cheeks and have gradually spread to involve the major portion of each cheek. There was no history of tuberculosis in the family, and the patient had no loss of weight, night sweats or fever.

Examination revealed an oval bright red area of dermatitis on each cheek about 3 by 2 inches (7.5 by 5 cm.). On diascopic pressure, small grayish yellow nodules were left, about 3 mm. in diameter. A roentgenogram of the chest did not reveal any evidence of tuberculosis.

Sections of a tiny piece of skin revealed a moderate parakeratosis. There was edema of the epidermis and marked edema beneath. There was a small conglomerate tubercle which contained giant cells, epithelioid cells and a fair number of lymphocytes. No acid-fast organisms were seen. Sections evidently represented a lesion of tuberculous nature of the lupus variety.

A tuberculin test with a dilution of 1:2,000 elicited a slightly positive reaction. The patient was given biweekly injections of old tuberculin beginning with a 1:10,000 dilution and increasing until 0.3 cc. of a 1:1,000 dilution was given. She also received unconcentrated liver extract intramuscularly. The eruption cleared completely in about three months, but one or two dime-sized lesions have reappeared since that time.

Six months ago a silver dollar–sized lesion developed on the left side of the jaw, a dime-sized lesion on each cheek and a similar lesion on the forehead. These have persisted in spite of treatment. A recent roentgenogram of the lungs revealed no evidence of tuberculosis. The sedimentation rate was slightly increased; the blood count was normal, and her general health was excellent.

A biopsy showed possible sarcoid structure.

Treatment in the last few months has consisted of heavy doses of ultraviolet radiation once a week and also injections of liver and bismuth once a week.

DISCUSSION

DR. MAURICE J. COSTELLO: I noticed on the left side of the cheek and chin old depressed scars as observed following lupus erythematosus.

DR. LESLIE P. BARKER: This case was presented because of the inflammatory character of the eruption and because it cleared up so quickly with injections of tuberculin, although the patient gave a negative reaction to a test with old tuberculin in a dilution of 1:1,000. Her face remained clear for about two years, when new lesions began to appear on the cheeks, chin and forehead, and they have continued to appear since that time. Injections of tuberculin have had no effect on the progress of the eruption since its recurrence.

A Case for Diagnosis (Reticulated Hyperpigmentation). Presented by DR. MAURICE J. COSTELLO.

A. B., a Puerto Rican housewife aged 38, from the outpatient department of Bellevue Hospital, presents a generalized, symmetric, nonpruritic eruption which has been continuously present for the past fifteen years. It consisted principally of reticulated areas of hyperpigmentation on a dull erythematous background confined to the affected areas. She complained of pains in the knees and ankles and swelling of the knees, ankles and finger joints. She has had attacks of angioneurotic edema and asthma. Her blood pressure was 160 systolic and 110 diastolic.

The Wassermann reaction of the blood was negative. Her hemoglobin determination was 70 per cent. The erythrocyte count was 4,710,000 per cubic millimeter and the leukocyte count 7,600, with a differential count of 58 per cent polymorphonuclear leukocytes, 37 per cent lymphocytes and 5 per cent eosinophils. Roentgenograms of the heart and lungs showed slight accentuation of the left ventricular curve, widening of the supracardiac aorta and diffuse congestive changes in both lungs. The basal metabolic rate on June 19, 1940 was +11 per cent and on July 26, 1939 +3 per cent. Roentgenograms of the hands showed no osseous changes. A patch test with tuberculin on the inner aspect of the left arm elicited a positive reaction and intradermal tests with old tuberculin in 1:1,000,000 and 1:100,000 dilutions elicited positive reactions.

DISCUSSION

DR. ROYAL M. MONTGOMERY: I think the condition is a melanosis. Many patients who have a reticulated type of dermatitis are photosensitive. I should think that Puerto Ricans, who are dark skinned, would not be so apt to be photosensitive.

DR. LAIRD S. VAN DYCK: This type of mottling suggests either poikiloderma or the pigmentation which may follow a dermatitis due to arsenic, gold or some other metal. The patient gives no history of any metallic medication.

DR. LESLIE P. BARKER: I think the condition in this case is poikiloderma and does not fit in with the picture of melanosis.

DR. MAURICE J. COSTELLO: Erythema and telangiectasia form a background for the reticulated hyperpigmented areas in this case.

Subcutaneous Fat Necrosis of the Newborn. Presented by DR. MAURICE J. COSTELLO.

Baby G., a 9 pound (4,082 Gm.) white boy, was born on Jan. 30, 1941, after seventy hours and thirty-five minutes of labor. The prolonged labor was due to the presence of a high transverse arrest with uterine inertia. Because of this, Barton's mid A forceps was applied and the child was delivered in the right occipitotransverse position. The mother of the child was a 31 year old primipara with a negative Wassermann reaction.

At the time of delivery a cephalohematoma was noted over the right occipitoparietal area. A roentgenogram of the skull was normal. On February 14 it was noted by the attending pediatrician that on the right cheek were "four distinct firm masses of various sizes, just below the zygoma and lowest submaxillary. These did not appear inflamed; the skin was not adherent, and they were not tender. The buccal mucosa appeared normal."

On February 23 the masses were still the same, and it was the opinion of the attending obstetrician at the time that they were "areas of fat necrosis caused by pressure from the forceps."

The next day I saw the patient. On the cheek there were four or five infiltrated, sharply demarcated plaques varying in size from half that of a dime to that of a quarter. These were noninflammatory clinically. There was a similar but larger lesion on the lower outer quadrant of the right buttock. A diagnosis of subcutaneous fat necrosis of the newborn was made.

On March 3 the patient was discharged with the masses of fat necrosis still present in the left cheek. Roentgenograms were taken of the lower jaw on February 29 but showed no evidence of any osseous or periosteal lesions. There was a slight thickening in the soft tissue below the jaw, but the cause could not be established from the roentgenographic appearance; there were no areas of calcification noted.

DISCUSSION

DR. LAIRD S. VAN DYCK: Is not this condition like chronic nonsuppurative panniculitis?

DR. MAURICE J. COSTELLO: Many obstetricians are not familiar with this condition, probably because it does not appear until about two to four weeks after birth, usually after the infant has been taken from the hospital, and it disappears after a few months. It is often seen in babies born after prolonged difficult labor. The infiltrated stony hard masses occur on areas subjected to pressure, such as the buttocks, scalp and face. Occasionally they are incised and drained on the erroneous assumption that they are due to a phlegmonous process. There is no residual atrophy or scarring. The infants presenting this condition are usually born at full term. Howard Fox (ARCH. DERMAT. & SYPH. **27**:237-250 [Feb.] 1933) stated that histologic examination shows changes in the subcutaneous tissue: "The essential process consisted of necrosis of subcutaneous fat cells with a granulomatous infiltration, in which giant cells predominated, containing needle-like crystals."

Interstitial Keratitis (Late Congenital Syphilis). Presented by DR. MAURICE J. COSTELLO.

E. C., a white girl aged 7 years, from the dermatologic service at St. Clare's Hospital, when admitted on Jan. 1, 1941, complained of tenderness and swelling over the pretibial area of the lower third of the left leg. About three weeks prior

to her admission she had been suffering from bilateral otitis media. She had pneumonia at the age of 3 months and a septic sore throat and pneumonia when she was 3 years old. She also had varicella and measles.

Ophthlmologic examination on January 10 by Dr. Kyle revealed that the lids of both eyes were normal. The left eye showed ciliary and conjunctival injection. The cornea showed an infiltration of its deeper layers extending from the upper third to the lower limbus. The pupil was contracted and did not react to light, as it was probably adherent to the anterior lens capsule. The fundus was not visible because of the contracted pupil and the infiltration of the cornea. The right eye showed a normal conjunctiva with a clear cornea, lens and vitreous. The retina did not show any pathologic changes. A diagnosis of interstitial keratitis and iritis of the left eye was made. Ophthalmoscopic examination on January 27 revealed that the left cornea previously examined showed further infiltration with a circular area of white precipitates and ciliary injection. The pupil was greatly contracted. The right eye showed beginning ciliary injection with infiltration of the cornea. The right pupil was contracted but not as greatly as the left pupil.

The Wassermann reaction of the blood was 4 plus, as was that of the mother and father, who are both under antisyphilitic treatment. On January 2 the blood showed: erythrocytes, 5,470,000; hemoglobin, 100 per cent; leukocytes, 27,000; polymorphonuclear leukocytes, 88 per cent (band forms 28 per cent and segmented forms 60 per cent); lymphocytes, 7 per cent; monocytes, 3 per cent; eosinophils, 1 per cent and basophils, 1 per cent.

A roentgenogram of the bones of the legs revealed syphilitic periostitis of both tibias, especially the left. During the first ten days in the hospital her temperature ranged from 100 to 102 F.

Local ophthalmologic treatment consisted of instillation of 1 per cent atropine sulfate, application of atropine ointment to the conjunctival sacs four times a day, hot wet compresses for a half-hour three times a day and 0.25 per cent pontocaine hydrochloride three times a day, 1 drop in each eye to relieve photophobia.

When the patient was first seen she had severe photophobia. She buried her head in the pillow constantly so that a traumatic eczema developed on the forehead and cheeks. The lacrimation was intense. She has shown remarkable improvement; the photophobia has practically disappeared, and visual acuity is returning.

The antisyphilitic treatment has consisted of weekly injections of neoarsphenamine, 0.2 Gm., and bismuth subsalicylate in oil, 1 cc. To date she has received twelve injections of each. She has also been given protiodide of mercury, ¼ grain (16 mg.) three times a day, a high vitamin diet and vitamin preparations by mouth.

DISCUSSION

DR. LAIRD S. VAN DYCK: The patient has shown a remarkable response to therapy in a relatively short time.

DR. ANTHONY C. CIPOLLARO: The thing that has impressed me about congenital syphilis is the fact that children so afflicted are usually keen and bright. The reaction time of the patient presented this evening is unusually rapid.

DR. LESLIE P. BARKER: I do not think one should feel too optimistic about the ultimate outcome in cases of interstitial keratitis, as there are apt to be recurrences. This patient has responded well to therapy, although photophobia is still present.

DR. MAURICE J. COSTELLO: The rapid favorable response to antisyphilitic treatment can be attributed to the fact that it was begun about two weeks after the first symptoms became manifest. The delayed time between symptoms and treatment is one of the factors in the persistence and resistance of this condition. I agree with Dr. Cipollaro about the reaction time in patients of this kind. They are precocious and their intelligence quotients are high. When children suffering with this condition are seen early and treated adequately, vision is not interfered with in the majority of cases.

Lupus Erythematosus, Acute Disseminated. Presented by Dr. Joseph C. Amersbach.

A. G., a woman, presents an eruption of two and one-half months' duration, involving the face, scalp, ears, chest, arms, hands and knees.

The patient had her tonsils removed thirteen years ago, at which time she had a slight fever and pain in the joints, apparently rheumatic fever.

The past treatment has consisted of intramuscular liver therapy.

The eruption consists of multiple erythematous, slightly scaly, irregularly circular, pea-sized and patchy areas on the face (especially on the sides), ears, left forearm and dorsa of the hands and knees; there are also a few on the scalp and chest. The lesions are bright red, but no atrophy is present. Follicular plugging is apparent in some of the lesions. The patient complains of pain in the right knee joint.

DISCUSSION

Dr. Laird S. Van Dyck: This condition is a beautiful example of acute disseminated lupus erythematosus. In my experience with similar cases no therapy has been very effective. Bismuth and gold compounds are usually contraindicated. One must search for a focus of infection, and in this case it appears to be an abscessed tooth.

Dr. Richard J. Kelly: This eruption resembles acute psoriasis and lichen planus, but the biopsy showed lupus erythematosus. I suggest that the patient be given high vitamin therapy, particularly vitamin B complex, and unconcentrated liver extract, as well as riboflavin and nicotinic acid, to see what benefit may result.

Dr. Maurice J. Costello: The interesting feature in this case from a clinical point of view is the itching and severe excoriation, which is unusual in this disease in my experience. The condition does not impress me as being the type of lupus erythematosus disseminatus that terminates in death. Treatment should be conservative. The administration of the gold salts is contraindicated. Daily injections of crude liver extract should be given. Sulfathiazole or another sulfanilamide derivative might be tried cautiously if the patient agrees to hospitalization.

Dr. Henry D. Niles: I agree with the previous speakers that injections of liver extract and massive doses of vitamin B by mouth are indicated. There should be a thorough search for foci of infection, and if any are found cultures should be made. It would be dangerous now to remove the foci in this case. As Dr. Costello suggested, I should give her sulfathiazole and vitamin B and then later remove the infected teeth.

Dr. Royal M. Montgomery: I was struck by the similarity of the lesions to those of psoriasis when I first saw the patient.

Dr. Franklin H. Grauer: I am inclined to agree with Dr. Costello. The eruption looks more like the disseminate variety of discoid lupus erythematosus (generalized discoid or chronic disseminate) or possibly the subacute disseminate variety, rather than the acute disseminate kind. Buschke was one of the first to speak of the treatment of lupus erythematosus with sulfanilamide. He found, I believe, that it was useful for the disseminate type but ineffective for the chronic discoid variety. O'Leary's experience with this drug in the treatment of lupus erythematosus at the Mayo Clinic has not been encouraging. Sulfanilamide tends to increase the average patient's sensitivity to light, and he therefore considered the use of such a drug for light-sensitive patients not warranted. This patient is said to have an old rheumatic heart. Sulfanilamide has also been used in the treatment of rheumatic fever. Has this patient's cardiac condition flared up recently with the onset of the present eruption? Her history suggests that the teeth might be a possible focus of infection, but as Dr. Niles said, they should not be extracted until the eruption subsides.

ATLANTIC DERMATOLOGIC CONFERENCE

J. HARPER BLAISDELL, M.D., *President*

BERNARD APPEL, M.D., *Secretary*

Boston, March 22, 1941

Sarcoid of Boeck. Presented by DR. BERNARD APPEL, Lynn, Mass.

E. L., a 40 year old woman, had a slowly growing "lump" on the lobule of the left ear which was treated by being "burned out" about four and a half years ago. It promptly recurred, and until the present treatment was instituted the lesion was growing slowly but progressively.

The lobule of the left ear is infiltrated with a soft tumor, producing enlargement to about twice the normal size. The skin is bluish pink, soft and smooth, with a loss of the normal architecture. The entire tumor mass is soft. On the flexor surface of the left forearm is a small nodule, 3 mm. in diameter, at the site of an intradermal test done one year ago. On the outer aspect of each arm is a bluish pink tumor about 1.5 cm. in diameter, nontender and adherent to the overlying skin.

A roentgen ray examination of the chest and hands showed no involvement. A guinea pig inoculated with a portion of material gave no evidence of tuberculosis on autopsy three weeks later. An intradermal test made forty-eight hours ago according to the Nickerson technic, with antigen, gave a positive reaction, which shows today on the right forearm as a dull red nodule about 5 mm. in diameter.

She received twelve injections of 0.1 to 0.5 cc. of phenylethylhydnocarpate (chaulmoogra oil esters) into the tumor. These injections caused no discomfort. There was a steady, definite though slow regression of the tumor so that it is now about two thirds of the size it was when first seen. She received the last treatment about one year ago.

DISCUSSION

DR. LEE MCCARTHY, Washington, D. C.: It is my impression that this condition is lupus tumidus with erythema of the ear. The histologic picture is typical of tuberculosis of the skin, with giant cells. I should like to call attention to the necrosis seen histologically, which certainly is not typical of sarcoid.

DR. EUGENE TRAUB, New York: The interpretation given by Dr. McCarthy is the one I feel is correct. The point which I wish to present is the treatment of this condition. I have had patients with lesions on the ears and nose who responded with excellent results to removal of the entire lesion in one sitting by means of the electric cutting current, with procaine anesthesia. A number of patients treated in this way have had no recurrence. When there was a question as to the removal being 100 per cent complete, this treatment was followed with roentgen ray therapy, which prevented recurrence. I think this might be done in this case, whether the condition is lupus or sarcoid.

DR. L. W. KETRON, Baltimore: Since it has been recognized that sarcoid is a systemic disease, one cannot always make a diagnosis from the cutaneous manifestations alone. Histologically there may be a typical picture of sarcoid of the glands and other structures with cutaneous lesions resembling lupus or other forms of cutaneous tuberculosis, or, on the other hand, a typical picture of sarcoid may be present on the skin with evidence of active tuberculosis of the internal organs.

DR. FRANCIS M. THURMON, Boston: I should like to ask Dr. Traub if similar treatment is advisable for lesions which lie adjacent to cartilage, as on the lobe of the ear.

DR. EUGENE TRAUB, New York: When the lesion is in close association with underlying cartilage, I don't think desiccation is a particularly good method of attack on lupus vulgaris. I have never used it. I use the electric cutting current.

DR. DONALD NICKERSON (by invitation), Salem, Mass.: Dr. R. H. Williams and I originated the test used in this case in 1935, basing it on the hypothesis that sarcoid is a virus disease. We prepared antigen on the idea of Frei's technic. The material used is from a cutaneous lesion of a patient in whose case the diagnosis has been established. Stains are made for acid-fast bacilli, and if such organisms are not present and if the material inoculated into guinea pigs gives negative results, we then feel we have a right to call the condition sarcoid. Antigen is prepared by mincing skin as finely as possible with the aid of sterile sand and making a final dilution of 1 to 6 with sterile saline solution. It is then heated at 56 C. for two hours one day and one hour the next day. Anaerobic and aerobic cultures are made, and if there is no growth the antigen is ready. As a control we usually use skin removed at surgical operations and treated the same way. I have used this test in about 20 cases and have obtained positive reactions. Injection is made intracutaneously with 0.1 cc. of the antigen. A positive reaction consists of a small nodule at the site of the inoculation, about 2 to 3 mm. in diameter with a surrounding erythema, 1 cm. in diameter, appearing in twenty-four to forty-eight hours. In some instances this fades at the end of five or six days and disappears. In half of the cases the lesions persisted for a long time. Examination of these sites of remaining reaction has shown a typical picture of sarcoid identical with the original lesions, and antigen prepared from these areas is also effective. I have injected the test material into patients with positive reactions to Frei's test and have never observed a false positive reaction.

This patient presents a microscopic picture of what is regarded as the active phase of sarcoid, with changes to which is applied the description "fibrinoid" deposit appearing in the centers of the lesions. Material taken for biopsy one year ago was injected into a guinea pig, and the reaction was negative for tuberculosis. Stains for acid-fast bacilli were also negative.

I have attempted to grow the virus on the culture medium originated by Dr. Hans Zinsser for typhus but have had no results. I have treated some patients with intracutaneous doses of this antigen over a period of months with good results; in 1 patient, with extensive lesions on the nose and cheeks which were identical with those of this patient, the condition cleared almost completely at the end of six months.

DR. LEON BABALIAN, Portland, Maine: Did you try the test in patients with tuberculous lesions or with lupus erythematosus?

DR. DONALD NICKERSON (by invitation), Salem, Mass.: Dr. John G. Downing would know better than I. He had a patient with lupus erythematosus whom I tested, with negative results. I have tested patients at a tuberculosis sanatorium in whom there was a question of tuberculosis or sarcoid by roentgen ray examination. I have obtained no positive reactions yet.

DR. MAURICE COSTELLO, New York: I wonder if constitutional and focal reactions to these intradermal tests have been observed in addition to the local test reaction, as are seen following the intradermal test with tuberculin.

DR. DONALD NICKERSON (by invitation), Salem, Mass.: As far as I know, there have been no constitutional reactions.

DR. BERNARD APPEL, Lynn, Mass.: It must be granted at the outset that clinically this lesion resembles tuberculosis. This resulted in a careful study for tuberculosis in the tissue removed. The guinea pig which was inoculated almost died of old age, and at autopsy no evidence of tuberculosis was found. Stains for tubercle bacilli were negative. Then the intradermal test, as just described by Dr. Nickerson, was made, and the result was positive; not only that, but the reaction has remained locally, definitely infiltrated at the site for almost one year,

which further substantiates the interpretation. Finally, the reaction shown today to a test which was made yesterday I should like to consider as specific, corroborating the diagnosis, in my opinion, of sarcoid.

Schaumann-Besnier-Boeck Disease, Boeck's Sarcoid (with Changes in the Bones). Presented by DR. JACOB H. SWARTZ, Boston.

H. J., a 42 year old woman, was admitted to the hospital in 1920, with a diagnosis of sarcoma of the left hand. Study, however, showed the condition to be tuberculosis, and a diagnosis of tuberculous dactylitis was made. In December 1921 she appeared with a lesion on the left cheek, of several months' duration, about 2 cm. in diameter. A clinical diagnosis of lupus vulgaris was made, and she was sent to Lakeville State Sanatorium, Middleboro, Mass. She was then treated locally with acid mercuric nitrate and was given ultraviolet irradiation, both general and local.

Roentgen ray examinations in 1922 showed tuberculosis of the bones of the hands. In 1923 roentgen ray examination showed cystic destruction of the bones of the hand. In 1922 a pathologic examination of some of the tissue showed tuberculous dactylitis. Between 1922 and 1930 she was seen at various intervals, receiving ultraviolet irradiation both locally and generally.

Roentgen ray examinations in 1933 showed multiple sharply defined cystic areas involving the first phalanges of the left thumb and first and fourth fingers. The first phalanx of the right fourth finger was affected. These changes involved the first, third and fifth metacarpal bones on the left and the ulnar styloid on the right. There was an old pathologic fracture through the first phalanx of the left index finger. The distal head of the fifth right metacarpal had been partially destroyed. The third and fifth fingers of the right hand have been amputated at the metacarpal phalangeal joint. The middle finger of the left hand has been amputated just distal to the head of the metacarpal. There was considerable soft tissue swelling about the first phalanx of the left index finger. The changes in the phalanges had more the appearance of a cystic disease than tuberculosis. There was, however, no generalized atrophy. The diagnosis at that time was "a question of osteitis fibrosa cystica; the changes in the fingers and chest also suggest the possibility of sarcoid."

A microscopic examination of tissue removed at operation from the finger of the right hand in 1922 showed a granuloma which had ulcerated the skin and extended through the underlying parts, composed of focal collections of epithelioid cells with an infiltration of lymphoid cells. An intradermal test with old tuberculin in dilutions of 1:40,000 and 1:10,000 gave negative results.

DISCUSSION

DR. DONALD M. PILLSBURY, Philadelphia: A feature of this case which interested me is the involvement of the rosacea areas of the face and the portion of the arms exposed to light. In the latter region it is noted that there is a sharp limitation of the lesions at the level of a short-sleeved dress. In sarcoid, as with so many other medical diseases with cutaneous lesions, there seems to be a tendency for the lesions to localize in areas of possibly lowered resistance, in this case in an area of vascular instability and one which is considerably exposed to sunlight.

DR. JACOB H. SWARTZ, Boston: I wonder about the growth of the eyelashes. She has had considerable difficulty with the lashes and comes in for epilation continuously.

Epidermolysis Bullosa. Presented by DR. F. P. MCCARTHY, Boston.

B. L., a 2 year old white child, has had a generalized eruption of bullous lesions since birth. The lesions are principally on the flexor surfaces of the elbows, knees and heels, in the oral cavity and on the back of the scalp. They

develop from the slightest trauma and are especially pronounced at areas of contact. There are atrophic lesions on the elbows, knees and heels, with dystrophy of the toe nails and finger nails. Minute cysts of the epidermis, coil and sebaceous glands can be seen microscopically. She has had a high vitamin diet, particularly vitamins B and D, and applications of gentian violet to the lesions with protection from trauma by padding of the knees and heels.

DISCUSSION

DR. JOHN G. DOWNING, Boston: I saw the child shortly after birth and obtained the history that she was born with lesions on the skin and mucous membrane. When she was bathed by the nurse one area of skin was rubbed, and shortly after that a bullous lesion appeared. This is the only case I have encountered in which lesions were present at birth. This case also presents an interesting social problem. I asked if the mother had any later pregnancies. She said no and that she would have no more children because of the possibility or probability of the next child's having the same condition. The family history shows that there is no tendency toward any cutaneous eruptions.

DR. F. P. MCCARTHY, Boston: The child was first seen at the hospital shortly after birth with the diagnosis of impetigo contagiosum. The knees and feet are kept padded, but new lesions are produced by trauma. Control of this progressive disease still baffles physicians. Suggestions for treatment are welcomed.

DR. E. LAWRENCE OLIVER, Boston: I have encountered quite a few cases of this condition in twenty-five years, and I recall only 1 or 2 in which there was a history of the condition's being hereditary. I recall 2 affected children in one family.

DR. DAVID BLOOM, New York: As epidermolysis bullosa is hereditary, prevention can be exercised only by enlightening the parents about the chances of their offspring being affected.

DR. J. LAMAR CALLAWAY, Durham, N. C.: I agree that the parents should be told that the disease is a hereditary abnormality of the skin and that measures should be taken to prevent further children. Recently I observed 2 children in the same family with the most severe type of epidermolysis bullosa.

DR. G. M. CRAWFORD, Boston: If one follows Cockayne's classification, there are five forms of epidermolysis bullosa, only one of which is inherited, and that as a recessive characteristic; it is the rarest type. This familial form never occurs in all members of a family and usually appears later in life. Unless a member of a family carrying the gene married a person carrying the same recessive gene, their offspring would not have the disease.

DR. AUSTIN W. CHEEVER, Boston: I know one family in which there are 5 in one generation, as well as several cousins, who have mild epidermolysis bullosa.

DR. F. P. MCCARTHY, Boston: The mother did ask about the advisability of having more children, and I indicated that the next child might have the same condition and left the decision up to the parents. I feel sure they do not intend to have another child. Incidentally, an older child, 5 years old, is normal.

A Case for Diagnosis (Lichen Planus? Lupus Erythematosus?). Presented by DR. C. GUY LANE, Boston.

N. A., a 45 year old woman, first noticed erythema with pruritus of the arms, neck and face in January 1939. She attributed this to the wearing of a fur coat, which she has since discarded. Three months later pigmentation of the cheeks, forehead and neck appeared. In March 1939 she complained of a sore mouth and there were lesions of the mucous membrane and small brownish, oval, discrete and coalescing dry lesions scattered over the sides of the neck and cheeks. There was a diffuse brown, violaceous pigmentation of the forehead and cheeks

extending over the mandible to the neck. On the cheeks the follicles were dilated and the skin atrophic. There were fine reticulated white streaks on each buccal mucosa.

The microscopic picture was consistent with a diagnosis of lupus erythematosus. From May to August she received fifteen intramuscular injections of a 3 per cent solution of mercury salicylarsenate, each 2 cc. From October to January 1940 she received ten intramuscular injections of bismuth subsalicylate in oil.

DISCUSSION

DR. L. W. KETRON, Baltimore: The histologic picture does not resemble that of either lupus erythematosus or lichen planus. I do not know what the condition is.

DR. LEE MCCARTHY, Washington, D. C.: The section from the buccal mucosa presents leukoplakia. I should like to ask if the section of the skin was taken in the acute stage of the disease.

DR. L. W. KETRON, Baltimore: The biopsy specimen seems to have been taken during a chronic stage of the disease.

DR. FRANK FRASER, New York: In regard to the lesions on the mucous membrane, I thought they resembled, as far as the gross appearance was concerned, lichen planus. In the slide which I examined the distribution and character of the inflammation seemed to harmonize with that diagnosis. The lesions on the face reminded me of those of 2 brothers who came under my observation at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. These brothers, after the administration of arsphenamine, had an eruption which was diagnosed clinically as lichenoid arsphenamine dermatitis. When histologic slides were examined, the picture in each case was identical with that of lichen planus. This brought up the question as to whether lichenoid arsphenamine dermatitis is a clinical or pathologic entity. According to the French school, it is not a clinical entity but a true lichen planus from hypersensitivity to arsenicals. My studies as well as those of my confreres in New York support that view. My diagnosis is lichen planus.

DR. FRANCIS A. ELLIS, Baltimore: Some years ago I looked up the literature on lichen planus for cases in which there were lesions on the face and could not find any. Recently an author reported 3 cases in which there were lesions on the face. In lichen planus a section from the mucous membrane usually is not as typical as one from the glabrous skin. Some drug eruptions due to gold, bismuth or arsphenamine mimic lichen planus clinically and histologically. Ordinarily in the sections there is more edema than one would see in lichen planus and the inflammation is not as well demarcated.

DR. A. ROSTENBERG, Washington, D. C.: I agree with Dr. Ketron. The condition also suggests the pigment anomaly known as Riehl's melanosis. The patient does not speak English well; accordingly I was not able to question her, but I suggest investigation along the lines of exposure to oil with ensuing pigmentary changes.

DR. F. P. MCCARTHY, Boston: In differentiating lichen planus from leukoplakia, the distribution is important. This woman wears upper and lower dental plates which are motile in the sense that she has "a hard time to keep them in." The distribution of the lesions is along the interdental line, which is subject to trauma. Leukoplakia may develop from poorly fitting plates in the absence of smoking. This patient also shows lesions on the tongue, and they are clinically more suggestive of lichen planus. It is difficult to differentiate between linear leukoplakia and lichen planus. The acanthosis of lichen planus is considerably more than in leukoplakia with hyperkeratosis. Frequently one sees an inflammatory reaction in the upper part of the cutis in leukoplakia that simulates the lesions of lichen planus. In spite of microscopic study, there are many cases in which one cannot differentiate between leukoplakia and lichen planus.

DR. FRED WEIDMAN, Philadelphia: According to the history, this patient received a bismuth compound, and I think one may conclude that bismuth, arsphenamine and gold can all produce lesions which correspond to lichen planus. I think that ordinary lichen planus can be excluded because the inflammation is not as deeply seated as shown in this slide. Perhaps the pigmentation is due to the bismuth. I wonder whether the condition began after the bismuth therapy was started.

DR. C. GUY LANE, Boston: Since the middle of 1939, when the patient first was seen, this condition has been, in my opinion, lichen planus. In fact, I have been using her for demonstration of lichen planus lesions. She has had flat, angular, shiny lesions on the flexor surfaces of the arms, neck and face and characteristic lesions in the mouth. Pigmentation, as I remember, developed late in the disease. She did not respond to twenty injections of mercury salicylarsenate. Later, bismuth therapy was started, and there was at least a little more in the way of fading of the lesions, although the pigmentation was much the same. I have not seen her for some time, and her lesions have faded considerably and do not show the amount of pigmentation of six or eight months ago. Some time ago I received a report of lupus erythematosus after a biopsy was performed. That question arose because of the butterfly distribution on her face. This case is a characteristic one, clinically, of unusual lichen planus of the face and neck.

DR. JACOB H. SWARTZ, Boston: As I remember, the patient had lesions similar to lichen planus clinically before bismuth therapy was started, and then the pigmentation appeared.

Darier's Disease (Keratosis Follicularis). Presented by DR. JACOB H. SWARTZ, Boston.

Since birth, C. H. O., a 12 year old white schoolboy, has had a nonitchy rash on his forehead at the hair line and in the postauricular areas. Little scabs form; these are picked off, and at times the sites bleed and ooze. His mother believes that certain foods, such as cream and chocolate cake, make the rash more pronounced. It is much worse in the summer. His mother has hay fever, but there is no other history of familial allergy.

On the forehead and behind the ears are raised erythematous papules which become confluent in spots. There are some thick crusts adherent to these regions. The areas behind the ears are similar. There is profuse scaling of the scalp. There are small pigmented areas running down from the areas behind the ears down to the shoulder. There are patches of brownish pigmentation in the axillas, on the hands, back of the neck, about the umbilicus and on the chest.

Ultraviolet irradiation made the condition worse. Local ointments, including salicylic acid and sulfur, were applied without beneficial results.

DISCUSSION

DR. ALBERT LEVENSON, Hartford, Conn.: I should hesitate to accept the diagnosis of Darier's disease. On the other hand, many features are present which are characteristic of that disease. The lesions on the exposed parts, namely, the flat, yellow, scaly papules which are almost verrucous in consistency are suggestive of epidermodysplasia verruciformis (Lewandowsky and Lutz), a rare dermatosis which may strongly simulate Darier's disease.

DR. FRANCIS A. ELLIS, Baltimore: Dr. Sullivan and I reported a case of epidermodysplasia verruciformis (ARCH. DERMAT. & SYPH. **40**:422 [Sept.] 1930). The condition in this case does not look like that disease, nor does the histologic picture suggest that diagnosis.

DR. DONALD PILLSBURY, Philadelphia: I should like to point out that the eruption was worse in the summer.

DR. SIGMUND GREENBAUM, Philadelphia: I wonder if any of the members present have been successful in the treatment of Darier's disease with vitamin A.

One patient in my care received 3,000,000 U. S. P. units of vitamin A for one month without any improvement in the lesions.

Dr. Jacob H. Swartz, Boston: I asked the patient about night blindness and other symptoms. There were none present. I have not started giving vitamin A.

Sarcoid. Presented by Dr. C. Guy Lane, Boston.

For three years, H. E. C., a 40 year old white man, a telephone worker, has had an eruption of redness over the anterior portion of each tibia which came on simultaneously and rather suddenly. According to the patient, "It seems as if one day they weren't there and the very next day they were there." If they have grown in size, the patient is unaware of it. He does not recall any trauma and has no knowledge of familial history of tuberculosis, diabetes or cancer. The lesions have caused him no subjective symptoms.

On the midportion of each tibia are sharply outlined areas of erythema with a surrounding purplish zone. The lesions are indurated with a firm waxy center. The color fades somewhat on pressure, and there is no telangiectasia. The edge of the liver is palpable 1 or 2 cm. below the costal margin.

Microscopic examination showed in the corium a rather dense acellular fibrosis and also numerous circumscribed focal collections of monocytes and giant cells in tuberculoid arrangement without caseation and with only slight lymphocytic infiltration about them. Such foci could not, so far as I know, be explained by a diagnosis of scleroderma and are definitely suggestive of sarcoid. A roentgen ray examination of the chest showed no abnormalities. A roentgen ray examination of the hands showed areas of rarefaction at the head of the middle phalanx of the left middle finger, which are consistent with sarcoid but not pathognomonic.

DISCUSSION

Dr. Henry B. Decker, Camden, N. J.: I saw the patient and cannot accept the diagnosis of sarcoid. The condition looked like a typical necrobiosis lipoidica diabeticorum. The man is a telephone lineman, and I wonder whether he could have had trauma in the involved area.

Dr. E. Myles Standish, Hartford, Conn.: Although the man is an employee of the telephone company, he says that he never climbs poles. He works at a desk all day.

Dr. Eugene Traub, New York: Conditions which later proved to be necrobiosis diabeticorum were first diagnosed by my associates and me as morphea or as granuloma annulare and sarcoid. It is unusual to see sarcoid on the lower extremities. Probably this condition will prove to be necrobiosis diabeticorum.

Dr. Francis A. Ellis, Baltimore: In reviewing the literature, I found that 30 per cent of the patients with necrobiosis lipoidica diabeticorum did not have diabetes. Boldt reported a series of 17 cases in 40 per cent of which there was no diabetes. Joslin in a personal communication stated that in his series of 23 cases of necrobiosis lipoidica diabeticorum the average age of the patients was 24 years. According to the literature, the lesions of necrobiosis lipoidica diabeticorum can be located anywhere, but they are prone to occur on the lower extremities. About 80 per cent of the patients were females. I had a patient in 1933 with a lesion similar to this one; it has now cleared up with roentgen ray therapy, and the patient still does not show diabetes.

Dr. C. Guy Lane, Boston: There was considerable discussion when this patient first came in, in regard to necrobiosis diabeticorum and scleroderma, but there was no history of diabetes. He is at present under investigation in the diabetic clinic in the hospital with reference to a prediabetic condition. I think the diagnosis of sarcoid is based on the microscopic picture and on the fact that one bony area in one hand shows rarefaction on roentgen ray examination.

Pemphigus Foliaceous; Sepsis with Pemphigoid Lesions. Presented by Dr. Edward Lafreniere, Arlington, Mass.

J. S., a 41 year old Jew, first noticed an eruption on his face in October 1940. He tried various local remedies, but the lesions continued to spread, particularly after he received an injection of tetanus antitoxin after stepping on a nail. He visited the Boston Dispensary from December 1940 until January 1941, where he received supportive treatment and 40 grains (2.5 Gm.) of sulfanilamide daily for five days; but the condition continued to progress downhill, and he was referred to the Boston City Hospital with a diagnosis of dermatitis herpetiformis or pemphigus. Since January 1941 there has been a slight degree of improvement.

He is well developed and well nourished, with a generalized eruption involving the face and trunk primarily. There are many large and small vesicles in the axillas, on the lateral wall of the chest and on the arms. Some of these have an areola around them, and others spring from normal skin. The face and trunk, anteriorly and posteriorly, present a mass of conglomerated blebs on an oozing, erythematous surface. Nikolsky's sign could be elicited. No oral lesions have been observed.

The white blood cells varied from 10,000 per cubic millimeter to 26,000. The blood smear was not remarkable except that there were 8 to 13 per cent eosinophils. The nonprotein nitrogen content of the blood was normal, but the ratio of albumin and globulin showed some disturbance: The albumin amounted to 3.8 Gm., 3 Gm., 2.7 Gm., 2.8 Gm., and 3.2 Gm. per hundred cubic centimeters, and the globulin, to 1.7 Gm., 1.9 Gm., 2.5 Gm., and 2.7 Gm. In January 1941 the calcium level of the blood was rather low, 6.6 and 7.8 mg. per hundred cubic centimeters, but it had increased to a normal of 13.4 mg. in March. The phosphorus and sodium values remained essentially normal. A blood culture showed Staphylococcus aureus. A microscopic examination showed fragmentation of the upper layers of the epidermis with moderate acanthosis, narrowing of the rete pegs and scattered lymphocytic infiltrate with increased vascularization. The result of a Pels-Macht test of the blood was 55 per cent and indicative of pemphigus.

He had a high vitamin and high caloric diet. He received 32 Gm. of sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine), 26 Gm. of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) and 20 to 30 capsules of vitamin D daily, each containing 50,000 U. S. P. units.

DISCUSSION

Dr. Edward Lafreniere, Arlington, Mass.: The calcium content of the blood has improved. The patient has a sense of well-being that he did not have before this therapy was started. How long this will last I do not know.

Epidermolysis Bullosa. Presented by Dr. C. Guy Lane, Boston.

Since birth E. D., a 17 year old white youth, has had lesions on every part of the body surface following the slightest trauma. The blisters are from 1 to 3 cm. in size and last for four or five days, then heal leaving a purple spot. He has no constitutional complaints. The family history is not significant. At present bullae of the mucous membrane of the mouth make it difficult for him to eat; the bullae on the conjunctiva disturb his vision, and those in the auditory canal impair his hearing.

Examination shows a thin, poorly nourished boy with polymorphous lesions on the skin with predilection for points of pressure. The lesions vary from purplish macules to clear or hemorrhagic bullae up to the size of a 25 cent piece to yellow crusted lesions and pinhead-sized pustules on the trunk. The lips, tongue and mucous membrane of the mouth show erosions. There are no finger nails or toe nails. The fingers and toes are dystrophic.

His basal metabolic rate was —17 per cent and —25 per cent on two occasions. Chemical examination of his blood showed 0.2 U. S. P. units of vitamin A per cubic centimeter, and the results of his gastrointestinal examinations were normal. He has received halibut liver oil and a high vitamin diet.

DISCUSSION

DR. F. P. MCCARTHY, Boston: This boy has had more or less continuous bullous lesions in the oral cavity with no evidence of scarring except on the floor of the mouth. He cannot protrude his tongue beyond the teeth, and there is a questionable scar of the soft palate. He shows progressive dystrophy of the extremities. The lesions tend to produce atrophy over the bony processes, particularly over the knees and elbows and arms, which are so badly involved that he has considerable difficulty in getting about.

Mycosis Fungoides. Epithelioma? Presented by DR. H. W. N. BENNETT, Manchester, N. H.

About five years ago J. C., a 59 year old white man, had an injury of the back of the right leg, which healed without difficulty. About five or six months later he noticed a raised red lesion in the vicinity of the original injury. Later other lesions appeared, but many of them have improved. Sixteen months ago a small lump was noticed on the lateral aspect of the left leg, on which a black crust developed. This lesion broke down and left a large ulcer, which has gradually increased in size.

On the anterior lateral aspect of the right thigh are large erythematous lesions which have slightly raised borders and atrophic centers. Many of them are covered with brownish scales. On the anterolateral aspect of the left thigh is a large fungating necrotic ulcer. The edges are piled up considerably, and in these crusted borders is seen considerable black pigment. The edges are undermined. The central area shows considerable granulation tissue which is bathed in pus. Several large nodular lesions are seen which seem to be extensions of the ulcerated lesion. There is a foul odor associated with the dermatitis. Two similar nonulcerated lesions are seen on the back.

The result of a Hinton test of the blood was negative. He has had two roentgen ray treatments without benefit. An ointment of allantoin with 0.5 per cent chlorobutanol was applied, with no effect.

DISCUSSION

DR. FRED WEIDMAN, Philadelphia: These lesions show secondary malignant changes. I should like to ask whether he has had arsenical therapy. This condition may be arsenical epithelioma.

DR. H. W. N. BENNETT, Manchester, N. H.: As far as I know the patient has had no arsenic. A question arose about exposure to coal tar compounds producing the so-called tar cancer, as the patient is employed in a gas works. This condition is not sarcoma, so the last clause does not apply. The case was presented because of the presence of all stages of mycosis fungoides in a single patient and not because mycosis fungoides is a rare condition.

Mycosis Fungoides. Presented by DR. JACOB H. SWARTZ, Boston.

E. C., a 62 year old white man, had a generalized eruption which began nine months ago (in May 1940) as scaling patches in the popliteal areas. Gradually the eruption spread down the legs to the feet. The arms and neck then became involved. In September 1940 the eruption oozed, and since October 1940 the skin has exfoliated.

There is a generalized erythroderma with lichenification and scaling. Alopecia of the scalp and eyebrows is present. There is hyperkeratosis of the nail bed

with lifting off of the nail plate in the region of the lunula. There are fissuring of the palms, oozing and edema of the legs and adenopathy of the axillas, groins and femoral region.

Microscopic examination of a lymph node showed chronic inflammation, and microscopic examination of the skin suggested mycosis fungoides.

He has received vitamin B complex, brewers' yeast and applications of a 30 per cent sulfur ointment without relief. Unfiltered roentgen ray treatments, about 60 r weekly, to the body have given some improvement.

DISCUSSION

DR. A. ROSTENBERG, Washington, D. C.: Clinically this condition might fit into an entity to which no definite name has been attached but which has been called by Sulzberger and Garbe exudative discoid and lichenoid chronic dermatosis. It is, I believe, an allergic dermatosis. It should be remembered that clinically conditions of this kind go through many stages; one stage resembles mycosis fungoides and often is diagnosed as such.

DR. FRANK FRASER, New York: I feel that this condition is not mycosis fungoides, but it may fall in the lymphoblastoma group. Generalized erythroderma and adenopathy are present. Adenopathy is usually a late feature in mycosis fungoides. There is no itching; itching does not always occur in that disease. In the cases which I have reported, in only 1 the condition began as generalized erythroderma. That feature is more suggestive of lymphatic leukemia. My diagnosis is lymphatic leukemia. The blood picture in this disease is secondary and due to metastases.

DR. C. GUY LANE, Boston: I have seen this patient in the ward and in the clinic. The condition impressed me as being in the leukemia group. I consider it as an example of the preleukemic stage of the skin with probable changes in the blood later.

DR. JACOB H. SWARTZ, Boston: I have watched the patient, and he has complained of itching. He had some roentgen ray therapy, which maybe explains the fact that he now has no itching. There was a great deal of discussion as to whether this condition was leukemia or mycosis fungoides. I can state that he had considerable scaling and a high degree of patches typical of mycosis fungoides.

Dementia Paralytica in a Patient Nine Years Old. Presented by DR. FRANCIS M. THURMON, Boston.

L. P., a 9 year old white boy, was admitted to the dermatologic clinic in December 1939, at the age of 8 years. Three weeks previously, at school, he fell and struck the right occiput, raising a lump on the scalp. Since then his gait has been uncertain and mentally he has seemed to go downhill. Up to this time his father had persistently refused to permit him to receive treatment. A serologic test of his mother gave a positive reaction for syphilis. She had received no treatment for syphilis when she was pregnant with the patient. One sibling died of pneumonia and congenital syphilis at the age of 1 month; no other children were born.

The patient is a friendly but mentally slow child. Both tympanic membranes are slightly retracted. The tonsils are hypertrophied, and a bifid uvula is present. The teeth are carious, and there is a slight notching of all central incisors. The face is slightly asymmetric, and there is a tendency toward sinking or saddle nose. The upper and lower deep reflexes are hyperactive and equal bilaterally. The Babinski test is positive bilaterally. The gait is uncertain and unsteady with the eyes closed.

The Hinton, Wassermann and Kahn serologic tests have given repeatedly positive reactions. The cerebrospinal fluid showed a total protein content of 50 mg. per hundred cubic centimeters. The reactions to the Davies-Hinton test and the Wassermann test of the spinal fluid were positive, and the colloidal gold

curve was 5555542100. He has received tryparsamide, mapharsen and a bismuth compound. Fever therapy was refused, and his condition has gone progressively downhill.

DISCUSSION

DR. BERNARD APPEL, Lynn, Mass.: I should like to say something about the colloidal gold curve in the spinal fluid, since there has been a recent tendency to discard it. The test should be retained as an important index in the administration of therapy. It is sometimes difficult to evaluate the effect of therapy otherwise.

A Case for Diagnosis (Anetoderma of Schweninger and Buzzi?). Presented by DR. M. M. TOLMAN, Boston.

C. E., a 44 year old white man, has had an eruption on the shoulders and back for about four years. This eruption came on suddenly, according to the patient; it appeared and developed within three days without any previous trouble and without itching, pain or other sensations. It has never bothered him in any way except for its appearance, and he has never submitted to an examination. He has latent syphilis and is receiving treatment.

There are closely grouped raised white soft plaques, 1 to 2 cm. in diameter and arising from normal skin without surrounding inflammation or evidence of a previous inflammatory process, extending on the back from the neck to the gluteal fold and fading onto the abdomen and shoulders.

The reactions to Wassermann and Hinton tests of the blood were positive. A roentgen ray examination of the chest showed in both lung fields an irregular increase of the pulmonary markings. There was no evidence of swelling of the glands in the hilus or in the mediastinum. The diaphragms were normal in shape. The observations are not characteristic of sarcoid; but they are suggestive of some generalized process, and sarcoid cannot be ruled out. The microscopic picture was typical of fibrosis.

DISCUSSION

DR. ANTHONY CIPOLLARO, New York: I cannot make a diagnosis as I have never seen anything like this condition.

DR. C. GUY LANE, Boston: I was surprised at the lesions on the back. My impression, seeing him today after one and one-half years, was that the lesions were more atrophic and wrinkled on the back. As I remember, the lesions on the back were more like the present ones on the shoulders.

Lupus Erythematosus Disseminatus (Subacute); Vitamin C Deficiency? Presented by DR. M. M. TOLMAN, Boston.

M. J. S., a 26 year old white woman, was previously presented before the New England Dermatological Society (ARCH. DERMAT. & SYPH. **43**:914 [May] 1941).

DISCUSSION

DR. DONALD M. PILLSBURY, Philadelphia: I do not see how one can differentiate between lupus erythematosus, pellagra and light sensitivity in this patient on the basis of the data presented. I believe that this patient's skin showed a favorable response after administration of vitamin B complex. Dr. Erich Urbach and I have been studying persons with light sensitivity and have observed increased amounts of porphyrin in the feces and in some cases an exaggerated change in the gastrointestinal flora, with a predominance of enterococci which seemed to be capable of forming porphyrin in vitro. A similar observation has been made in some cases of lupus erythematosus. Occasionally patients with this condition will respond to adequate doses of vitamin B complex, to the administration of hydrochloric acid if there is achlorhydria or to something which will change the gastrointestinal flora, such as acidophilus milk. Such therapy is by no means always successful but is definitely worthy of trial.

DR. J. LAMAR CALLAWAY, Durham, N. C.: In the past three years I have seen 11 patients with acute lupus erythematosus disseminatus who despite treatment with sulfanilamide or one of its derivatives, blood transfusions and supportive therapy have all died within six months after the diagnosis was established.

DR. EUGENE TRAUB, New York: It seems to me that there is frequently a history of arthritis, and this has to be considered as well as the bad prognosis. More and more cases of this condition are observed; in some it is fatal. In these cases there are hemorrhages into the skin and in most of them leukopenia and some anemia. Sulfathiazole therapy is dangerous and may precipitate a fatal outcome. Transfusions are of benefit. I had a patient who I thought surely would die but who after receiving transfusions became better and went home. Patients with this condition should be treated as medical patients rather than on a strictly dermatologic basis.

DR. MAURICE COSTELLO, New York: I should like to ask whether this patient received sulfanilamide before this eruption appeared. A patient I observed was given sulfanilamide tablets and was told to avoid sunlight. Two months later, in early September, when she thought it was safe, she exposed her body to the sunlight and disseminated lupus erythematosus of the subacute type developed.

DR. M. M. TOLMAN, Boston: No sulfathiazole was given to this patient.

Pili Torti; Ectodermal Dysplasia. Presented by DR. BERNARD APPEL, Lynn, Mass.

C. F., a 10 year old white girl, has had diffuse alopecia since birth. The hair has been dry, lifeless and crinkly. During the last two months a patch of thinning-out of the hair on the vertex of the scalp has developed. Her father, paternal grandfather, brother and sister have the same type of hair.

There is a general thinning-out of the hair. The area of alopecia in the center of the scalp has short hairs, broken about ½ inch (1.3 cm.) from the scalp. The skin is smooth with no signs of inflammation or scarring. The outer two thirds of the eyebrows are almost bald. The teeth are slightly notched and show a yellowish discoloration of the dentine where the enamel is lost. There are no other signs of ectodermal dysplasia.

Microscopic examination of the hairs reveals twisting. The reaction to a Hinton test of the blood was negative.

DISCUSSION

DR. F. RONCHESE, Providence, R. I.: The clinical appearance in this case is exactly like that in one I presented in 1931 before the New England Dermatological Society and of which I later published a report (ARCH. DERMAT. & SYPH. **26**:98 [July] 1932). I have seen my patient several times in the last ten years, and at present one has to look at her hair closely to notice the abnormality. She is able to dress her hair almost like that of other women.

Lichen Spinulosus. Vitamin A Deficiency? Presented by DR. W. T. GARFIELD, Boston.

E. B., a 37 year old white woman, has had a moderately pruritic eruption on her back and arms for about six or eight months. Night blindness is present.

There is a grouped, hyperkeratotic follicular eruption with occasional spinous projections on the back and a few scattered areas on the arms.

A microscopic examination showed moderate hyperkeratosis with slight atrophy of the epidermis and great dilatation of the follicles, which were filled with masses of horny material, and a moderate amount of perifollicular infiltration of small lymphocytes.

She has received halibut liver oil capsules, 6 each day, 60,000 U. S. P. units of vitamin A and 1,500 U. S. P. units of vitamin D, with definite improvement.

Polyvitamin Deficiency; Lichen Spinulosus. Presented by DR. WALTER GARFIELD, Boston.

H. E., a 38 year old white man, has had a rash on his back, arms and lower extremities for the past two months without any particular associated symptoms. His diet has been fairly adequate and alcoholic ingestion moderate.

The patient presents moderately hyperkeratotic lesions about the hair follicles with some spinous projections, limited mostly to the arms and trunk. His tongue is smooth, shiny and moderately reddened. There are several purpuric, follicular lesions with keratotic plugs on the extensor surfaces of the legs.

A Hinton test of the blood gave a negative reaction, and microscopic examination of a piece of tissue showed moderate hyperkeratosis with dilated follicles filled with masses of horn. There was a moderate amount of perifollicular infiltration of lymphocytes, with atrophy of the sebaceous glands.

He has received an adequate diet, 1 capsule of vitamin B complex three times a day and a fish liver oil preparation (navitol), as a source of vitamins A and D, three times a day. The condition of the tongue and the keratotic lesions on the legs have improved.

DISCUSSION OF TWO CASES OF LICHEN SPINULOSUS

DR. MAURICE SULLIVAN, Baltimore: It is incorrect to base a diagnosis of vitamin deficiency entirely on macroscopic changes in the skin. I am frequently amazed at the ease with which the internist is able to make clinical diagnoses, such as cheilitis due to ariboflavinosis and phrynoderma due to vitamin A deficiency. By contrast, the dermatologist usually is reluctant to accept the diagnosis of vitamin deficiency based on a morphologic alteration which bears a slight or indeed even a striking resemblance to the lesion reported to be characteristic of a certain deficiency. The dermatologist recognizes that there are many lesions which may confuse the enthusiast who sees in every dilated follicle a hyperkeratotic plug for vitamin A deficiency and who smiles knowingly at each commisural fissure as he prescribes riboflavin. Then, too, the dermatologist appreciates microscopic as well as macroscopic minutiae which often confirm a diagnosis. Many tiny details regarded as important to the dermatologist fail to impress and often amuse physicians other than dermatologists. There is frequent conflict between the dermatologic and medical consultants concerning diagnoses of vitamin deficiencies. So often has a so-called deficiency syndrome proved to be a well known dermatologic entity which persists in spite of vitamin therapy that some skeptical dermatologists doubt the existence of such syndromes. This attitude is unfortunate, because in the nutritional approach to dermatology there must be some answers to problems which suggest that the causes of at least a few cutaneous diseases are wholly or partially nutritional. Before it is possible to solve these problems it will be necessary to clarify the mode of action of vitamins in the experimental animal. There are sufficient data to demonstrate the importance of adequate nutrition for the maintenance of the integrity of the skin of the rat. Omission from the diet of a rat of certain vitamins results in gross and microscopic changes in the skin which are characteristic. It is hoped that in a few years, when biochemists will have synthesized vitamins yet unknown, there will be more concrete knowledge of their applicability in clinical dermatology.

I should not be willing to accept the diagnosis of "polyvitamin deficiency" on the basis of the clinical observations and certainly not on the history in this case. The patient's diet, although far from ideal, is not inadequate enough to account for the widespread eruption. He appears to be in excellent health. He is certainly adequately nourished. He has no symptoms referable to gastrointestinal disease. If a biopsy section showed changes suggestive of vitamin A deficiency there might be more point to the diagnosis.

A Case for Diagnosis (Dermatitis Actinica?). Presented by DR. WILLIAM P. BOARDMAN.

When first seen, in September 1939, M. McK., a 47 year old white woman, had blebs on the extensor surfaces of both forearms and the dorsa of the fingers, with red marks of previous lesions. There were no areolas around the blebs. She was treated with wet dressings and told to abstain from feen-a-mint, which she had been taking every other day. The lesions cleared up completely in November 1939.

She was given 2½ grains (0.15 Gm.) of phenolphthalein as a test dose. One week later she returned with a recurrence of the lesions on the hands and forearms and with a complaint of being ill for two days after taking the medicine. She continued to have occasional lesions until December 1939 without taking phenolphthalein. She returned again this year when the hot weather started and stated that the condition recurred on exposure to the sun. At this time she had lesions on the extensor surfaces of both forearms, legs and hands and a few on the face. In February 1941 a new type of lesion appeared on the dorsa of the fingers.

Examination shows many large and small oval hyperpigmented depressed scars on the extremities, particularly the extensor surfaces. On the dorsa of the fingers are many hard, pinhead-sized, whitish lesions in groups.

A microscopic examination showed severe hyperkeratosis with flattening of the epidermis and several large cystic areas beneath the basal layer lined by epithelial cells and filled with a horny material.

DISCUSSION

DR. J. ELLER, New York: I should like to suggest a diagnosis of epidermolysis bullosa because the lesions apparently follow trauma.

DR. WILLIAM P. BOARDMAN, Boston: The lesions appeared first after ingestion of phenolphthalein, and there was no history of excessive sunlight. There is no history of trauma consistent with epidermolysis bullosa.

Naevus Verrucosa Linearis Associated with Lipomatosis and Possible Neurofibromas. Presented by DR. M. M. TOLMAN, Boston.

R. A. R., a 43 year old white woman, was admitted to the surgical service on Dec. 20, 1940 with a strangulated sigmoid flexure, which also showed adenocarcinoma. Since birth she has had linear pigmented verrucous lesions on the left side of her body and fatty tumors on both legs and the left hip. She has also had three areas of pigmentation in both axillas, which she associated with her use of crutches. These have been present for twelve years. She has had numerous surgical and plastic operations on the feet, removal of fatty tumors, acute diverticulitis and minor amputations.

Examination shows an extensive unilateral verrucous nevus limited to the left side of the body and on the buttocks. Both axillas showed symmetrically dark brownish pigmentation with small papillomatous smooth outlines. The legs showed diffuse multiple lipomas.

A microscopic examination of a lesion from the axilla showed "hyperkeratosis with no diagnostic abnormalities." The values for cholesterol and total fat were normal. A roentgen ray examination of the pelvis showed numerous defects suggestive of multiple neurofibromatosis.

Anetoderma of Schweninger and Buzzi; Acne Vulgaris. Presented by DR. JOHN G. DOWNING, Boston.

G. P., a 15 year old white girl, has had pustular lesions on the thighs, buttocks and back for many years. In the last few years she has noticed that these lesions heal, leaving a white scar which presents a lessened resistance to palpation.

She has a severe acneform eruption on the back. The lesions are large and form abscesses. Several large and small oval lesions are present in the post-axillary line and on the inner surfaces of the thighs. The surface of these lesions is shiny, white and scarlike, with a lessened resistance on palpation and occasional herniation. A microscopic examination showed atrophy of the epithelium and collagenous thickening of the corium. There was slight chronic inflammation of the corium. There were no vascular changes.

Lichen Sclerosus et Atrophicus. Presented by DR. BERNARD APPEL, Lynn, Mass.

D. M., a 45 year old white woman, has had an eruption on the neck, in the clavicular areas and on the lower extremities for one and a half years. This started as insidious, nonitching lesions which have undergone a slow but continuous change from pink dry "pimples" to smooth white spots on the neck and which have changed from button-like brown dry lesions to scaly white areas on the inner aspects of both knees. None of the lesions have ever been itchy.

On the neck and in the clavicular areas are scattered, discrete, white, smooth, shiny, atrophic, macular lesions varying from 3 mm. to 2 cm. in diameter, following along the lines of cleavage of the skin over the clavicles. Some of the smaller lesions which are papular have a tendency toward annular form. There are extensive, white, smooth, atrophic, macular, psoriasiform areas on the knees which are linear in shape and measure about 2 by 4 cm.

A microscopic examination of the lesions showed thinned, atrophic epithelium with subpapillary infiltrate of lymphocytes.

She received seven intramuscular injections of bismuth subsalicylate in oil with no arrest in the progress of the lesions. There was no improvement after two intravenous injections of neoarsphenamine of 0.1 and 0.3 Gm. respectively.

DISCUSSION

DR. SIGMUND GREENBAUM, Philadelphia: Although a diagnosis of lichen sclerosus et atrophicus has been made, the lesions are characteristic of lichen planus.

DR. FRANCIS ELLIS, Baltimore: I agree with the diagnosis as presented. The histologic picture is like that described by Montgomery and Hill (ARCH. DERMAT. & SYPH. **42**:755 [Nov.] 1940) with the characteristic changes below the epidermis. The collagen is rarefied, as in this case, and suggests edema.

DR. FRED WEIDMAN, Philadelphia: The condition in this case is typical of lichen sclerosus et atrophicus clinically and histologically. I examined the lesions with a pocket magnifying lens, particularly the periphery of the early lesions, and could detect a degree of translucence. This is a fine observation, but I thought I saw it and wonder whether it occurs consistently in this entity. When I pressed with the finger nails, I could get wrinkling.

DR. BERNARD APPEL, Lynn, Mass.: Microscopically the picture of the lesions fits in best with lichen planus. The small annular type of lesions which have a crinkly surface would resemble the clinical type of papular lichen planus. I wonder if it would be a breach of modern nomenclature if "lichen planus" had been allowed to remain as the diagnosis. Because of the collagen changes in the subepithelial spaces, the term "sclerosus et atrophicus" is justified.

Pemphigus Erythematosus; Sulfathiazole Rash. Presented by DR. GEORGE SCHWARTZ, Boston.

E. B., a 38 year old white woman, noticed a rash on her face about five or six months ago. Lesions appeared on the trunk several months later, and she has had occasional lesions in the mouth.

She is well developed and well nourished, apparently in good health and fever free. She presents a butterfly-shaped lesion on the nose and cheeks which is

characterized by erythema, infiltration and dilatation of the follicles. There are several scattered erythematous scaly plaques on the neck. The trunk, both anteriorly and posteriorly, presents an erythematous oozing, scaling dermatitis. There are several scattered papular lesions with flaccid bleb surfaces on the extremities. The Nikolsky sign was positive.

The blood chemically and morphologically was normal. The Pels-Macht test gave a "phytotoxic index of 59 per cent, which shows that the serum is quite toxic and falls in the pemphigus class." The microscopic examination showed distortion and fragmentation of the upper layers of the epidermis. In one area was a suspicious-looking bleb filled with dried serum and a few polymorphonuclear leukocytes. lymphocytes and eosinophils. There was increased vascularization in the corium, with scattered infiltrate of lymphocytes and eosinophils.

She has been on a high caloric and high vitamin diet. She received 14 Gm. of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) from February 27 to March 1, 1941. A drug rash developed, and administration of the drug was discontinued. The lesions seemed to progress after this. On March 6 sulfanilamide treatment was instituted, 6 Gm. being given daily. On March 11 a drug reaction developed with fever, nausea and vomiting, and administration of the drug was discontinued.

DISCUSSION

DR. GEORGE SCHWARTZ, Boston: First there was a question of vitamin A deficiency, and this patient received large doses of vitamin A for a number of weeks without results. I first saw her on Jan. 2, 1941, with seborrhea of the scalp and a few lesions between the breasts and over the sacrum. Two weeks later a patch 1 cm. in diameter resembling lupus erythematosus appeared on the right cheek; later the other lesions developed.

Dermatitis Medicamentosa from Dilantin Sodium (Unilateral Acneform Eruption and Hyperplastic Overgrowth of Gums). Horner's Syndrome. Presented by DR. F. P. MCCARTHY, Boston.

L. R., a 22 year old white girl, was first seen in 1930 with jacksonian epilepsy. In 1932 a right cervical sympathectomy was performed, which produced Horner's syndrome on the right. She continued having epileptic seizures until February 1940, when she was given increasing doses of dilantin sodium until a maintenance dose of 0.4 to 0.5 Gm. daily was attained in June 1940. In July 1940 a rash developed on her face, together with beginning overgrowth of gum tissue around the upper and lower teeth and an acneform eruption on the side opposite the one on which sympathectomy had been done.

She presents Horner's syndrome on the right side (mycosis, ptosis and enophthalmos) and a unilateral acneform eruption on the left cheek and on the chin. This rash is characterized by granulomatous, hyperplastic, cystic tissue which is secondarily infected. Both the lower and the upper gum present hyperplastic overgrowth.

A microscopic examination showed light acanthosis of the epithelial surface. The tunica propria showed a dense infiltration with lymphoid and plasma cells and some polymorphonuclear leukocytes and increased vascularization of the gum. The picture was consistent with a nonspecific inflammatory process. The skin of the face showed an epidermis with considerable hyperkeratosis and surface invagination, which was thinned out, with obliteration of rete pegs. A cellular infiltrate was present in the corium, consisting mainly of lymphocytes, with some giant and epithelioid cells, being more pronounced about the vessels and sebaceous glands. The process was apparently not a specific reaction.

DISCUSSION

DR. FRED WEIDMAN, Philadelphia: It is interesting indeed to find a drug producing hyperplasia of this sort. It puts one on the way to understanding other conditions producing hypertrophy.

DR. BERNARD APPEL, Lynn, Mass.: I should like to point out that many of the lesions were on both sides of the chin. This would tend to rule out Horner's syndrome as a cause. Dr. H. H. Merritt, of the neuropathologic department of the Boston City Hospital, one of the codiscoverers of the drug, who has probably seen more of the reactions to it than any one else, admitted that it has often produced acneform lesions on the glabrous skin. He has seen the hyperplasia on the gums and considers this as consistent with the effect of the drug. My impression is that the lesions are now from one third to one fourth the size that they were at the time when the patient was receiving large doses of dilantin sodium.

A Case for Diagnosis (Blastomycosis? Actinomycosis?). Presented by DR. G. M. CRAWFORD, Boston.

T. J. C., a 70 year old white man, who has been an acid mixer for fifty years and in constant contact with the fumes of sulfur, ethyl nitrite and phosphorus, had a large egg-shaped swelling on the left temple. This area was incised and apparently healed. Twenty-nine years ago the patient had a crust 1 by 1½ inches (2.5 by 4 cm.) on the left temple with a draining sinus at the lower border which led to the bone. A similar sinus was found on the left side of the tip of the chin. These were surgically drained, and a diagnosis of actinomycosis of the forehead was made, apparently without laboratory confirmation. Twenty-eight years ago, because of continued drainage of the wound in the left frontal area, curettage of the left frontal sinus was performed. Three years later the patient had an abscess of the left forearm, which was incised and drained. Two years later a profuse right nasal discharge led to opening, incision and curettage of the right frontal and both ethmoid sinuses and the right antrum, and nine years later the right eye was removed. A biopsy specimen was taken from the remains of the sinus about six years ago, but the report was "nonmalignant." One month later roentgen ray therapy was started, which he has received since then at intervals. Four years ago a second biopsy showed no evidence of blastomycosis or malignant change. Two years ago cultures showed no organisms. He was admitted to the hospital one year ago because of continued activity of the condition and because of only temporary relief with roentgen ray therapy and large doses of potassium iodide.

Examination reveals an empty right orbit with a considerably enlarged cavernous opening. It is surrounded by a dull red zone 1 to 2 cm. in width which is studded with numerous small pustules and shows some crusting. There are a few small shotty glands in the neck. The exposure of the right orbit extends to the bone in all directions and into the ethmoid sinus. The latter and the posterior nasal structures show a smooth pink granulating membrane. All cultures were negative. Treatment has consisted of large doses of roentgen rays, massive doses of potassium iodide, an intensive course of sulfanilamide therapy and various combinations of local treatment.

DISCUSSION

DR. F. J. EICHENLAUB, Washington, D. C.: The condition in this case is a definite infection with actinomycotic organisms.

DR. F. J. EICHENLAUB, Washington, D. C.: I do not see how this case can be accepted as a definite instance of either blastomycosis or actinomycosis without cultures of one or the other of the organisms.

DR. G. M. CRAWFORD, Boston: When I first saw this patient about seven years ago, he presented essentially the same picture as he does today. When he first came to the Massachusetts General Hospital, in 1912, with a draining sinus, the diagnosis of actinomycosis was made, although the record shows no laboratory proof. About 1936 blastomycosis crept into the record for some unknown reason, and this has never been proved either.

Recurrent Vesicular Eruption of the Hands Associated with Menses and Low Estrogen Level in the Blood. Presented by DR. JOHN ADAMS, Boston.

M. R., a 29 year old white woman, had an eruption on the right hand which developed in July 1930. The left hand became involved soon after that. There were no subjective symptoms until 1931, when the eruption became pruritic. The dermatitis has flared up with every menstrual period during the past ten years, usually beginning one week before the period and subsiding two weeks later. Between the flare-ups, however, a few papules persist on the dorsa of the hands. During 1938 and 1939, when the patient's menstrual flow increased without known cause, she was free of the eruption. She has been married for six years and has never been pregnant. Her periods are regular. There is a scanty flow for one day, and she has cramps for about one week. The breasts become sore and swollen. She had a severe outbreak on the hands in May 1940, with cellulitis and fever.

There are a few deep-seated vesicles on the webs and discrete pinhead-sized papules on the dorsa of the hands.

The results of assays for 17-keto steroid were 5.7 mg. and 4.7 mg. per twenty-four hours.

DISCUSSION

DR. DONALD PILLSBURY, Philadelphia: The relation of exacerbations of this patient's cutaneous condition to the menses is extremely interesting. I suggest a trial of estrogenic substance to determine if the exacerbations can be related to an increased level of this hormone in the blood at that time. The condition on this patient's hands is typical of a group of diseases which I am sure most dermatologists have found to be extremely resistant to treatment. I believe that two measures might be worth while: The first is an attempt to determine whether or not a toxin is present in the blood stream at the time of the menses; and if the patient is found to be sensitive to it, efforts at desensitization might be made according to the method outlined in a recent article by C. C. Thomas (ARCH. DERMAT. & SYPH. **43**:817 [May] 1941) in the treatment of a patient with herpes simplex recurrent with the menses. The second measure, in view of the suggestive herpetiform character of the patches on the hands in cases of this type, is to try experimentally a series of injections of cowpox virus. Certainly the local treatment of these lesions is most disappointing.

Sarcoma of Kaposi. Presented by DR. G. M. CRAWFORD, Boston.

M. M., a 54 year old white woman, first noticed a small "black and blue spot" on the inner aspect of the midportion of the left calf about two years ago. The spot gradually enlarged, and she began to have similar spots over the entire leg. These started with pinpoint-sized lesions which were dark blue and gradually enlarged and became raised above the level of the skin. Three months ago, she noticed bluish discoloration of the right sole, and soon the entire foot began to swell and the toes became involved. A small lesion appeared on the upper part of the right arm later.

When she was first seen, there were patchy areas of bluish infiltration on both soles, the dorsa of the toes, the legs, the thighs, the buttocks and the right arm.

The diagnosis after a microscopic examination was "Angioma; sarcoma consistent with Kaposi's disease."

She has received roentgen ray therapy from Sept. 2, 1938 through October 1939 with great improvement but not complete eradication of the lesions.

DISCUSSION

DR. FRED WEIDMAN, Philadelphia: This subject was called to the attention of mycologists by a recent report by Greco, Bigatti, de Leon and Capurro, (*Rev. Asoc. méd. argent.* **53**:567 [July] 1939) in which a cryptococcus was found (Cryptococcus haematicon). These structures were, in my opinion, artefacts.

Granuloma Annulare. Presented by Dr. John Adams, Boston.

R. C., a 25 years old white woman, had blisters on the fingers of the right hand twenty years ago which developed following cigaret burns. The blisters did not break but became hard and spread peripherally. These lesions disappeared spontaneously five or six years later. Fourteen years ago similar lesions recurred limited to the knuckle of the right index finger. These have persisted unchanged to the present. Six months ago new lesions were noted on the sides and dorsum of the right fourth finger. Others have since been noted on the middle and right index fingers. Two months ago the lesions appeared on the thumb and index finger of the left hand. Her hands were frostbitten seven years ago.

Her hands and feet are cold. On the dorsa and sides of the thumb, index finger, middle and fourth fingers of the right hand and the thumb and index finger of the left hand are discrete and grouped, firm, white, waxy papules, 2 to 8 mm. in diameter, round, half-moon and kidney shaped. Some have a dome-shaped top, and others have a central depression with a hyperkeratotic adherent crust. All the lesions are in the region of the joints.

A microscopic examination showed a picture consistent with but not typical of granuloma annulare.

Hemiatrophy: Left Side of the Face, Left Thigh and Left Leg. Presented by Dr. Francis M. Thurmon, Boston.

M. I., a 40 year old white woman, has had hemiatrophy of the face, left thigh and leg since early childhood. However, her chief complaint is a gain in weight from 180 to 208 pounds (81.5 to 94 Kg.) within the past month. She feels generally run down and fatigued. She had the usual childhood diseases, pneumonia and empyema with rib resection and drainage at the age of 7 years, "scarlet fever" six years ago and an ischiorectal abscess drained four years ago. She has had four normal deliveries. There is no family history of hemiatrophy. There have been no convulsions, facial palsy, epilepsy or demonstrable disease of the central nervous system.

There is a depression of the skull at the midline of the vertex. There is a depression supraorbitally of the frontal bone on the left. There is a depression of the left cheek and a loss of subcutaneous fat, giving the entire face an asymmetry. The entire left leg is smaller in circumference than the right leg. There is muscular atrophy with thickening and fibrosis of the muscles over the medial surface of the left thigh, while the overlying skin shows a sclerodermatous change. This process extends from the knee to the groin. The deep reflexes are normal, and there are no sensory disturbances.

Serologic reactions were negative to the Wassermann and Kahn tests but positive to a Hinton test on one occasion and doubtful on another. The microscopic examination of a section of tissue from the thigh stained with eosin and methylene blue, one section stained with Mallory's connective tissue stain and one section stained with Verhoeff's elastic tissue stain showed moderate atrophy of the epidermis and a thin layer of keratinized epithelial cells adherent to the prominent stratum lucidum. The corium was slightly edematous. A few inflammatory cells were found around occasional blood vessels. There was atrophy of the cutaneous appendages, only a few sweat gland structures being present. No hair follicles or sebaceous glands were seen. Deep in the corium and in the adjacent fatty tissue there were several prominent arterioles in the thickened hyperplastic and hypertrophied muscular walls. There was no inflammatory cell infiltration of the walls of these vessels or their adventitial coats. The two outstanding features were the atrophy of the epidermis and cutaneous appendages and the hyperplasia and hypertrophy of the smooth muscle of the walls of the arterioles.

DISCUSSION

Dr. Francis Thurmon, Boston: This case was presented merely because of the rarity of the condition and to call attention to the fact that it can involve

half of the body. Histologically, I thought the outstanding features were the atrophy of the epidermis and cutaneous appendages, and I wonder if possibly it might be proved to be due to atrophy or sclerosis in the epidermis.

Poikiloderma Atrophicans Vasculare (Jacobi). Parapsoriasis? Presented by DR. G. M. CRAWFORD, Boston.

In 1920 a dry scaly patch first appeared on the left thigh of R. S., a 51 year old white woman. This lesion spread peripherally, and within a year the right thigh was also involved. Then the eruption appeared on the buttocks and breasts. By 1927 the lesions were noted on the arms. The eruption has been stationary for about two years and fades out somewhat in the summer. During the winter the patient notices itching, scaling and "chapping" of the lesions. The eruption has never disappeared.

On the inner surface of the arms and extending to the axillas are irregular, smooth, pigmented and telangiectatic patches between which the skin is also pigmented. The entire breasts show reticulated, erythematous atrophic lesions. There are scattered, scaling patches over the abdomen and thighs. The buttocks are completely involved by a red scaling eruption. On the lower part of the back there is increased spotty brownish pigmentation.

DISCUSSION

DR. EUGENE TRAUB, New York: Poikiloderma atrophicans vasculare (Jacobi) is, in my opinion, a fairly good descriptive term designating a phase or stage in this patient of lymphoblastoma or mycosis fungoides.

Xanthoma Tuberosum Multiplex. Presented by DR. M. M. TOLMAN, Boston.

T. L., a 37 year old white man, began to notice the present eruption at the age of 14 years, when it first appeared on the right elbow. The spread was insidious and gradual. It appeared on the hands at the age of 23 and has had its greatest spread in the last five years. He has noticed the most rapid growth over the points of pressure. At times the lesions have caused some pain. His grandfather and grandmother had diabetes. He had jaundice for four days as an infant. He has always liked fatty food—chocolates, peanut butter, butter and nuts.

On the palms, fingers, elbows, knees and buttocks are numerous nodules varying from the size of a pea to a large tumor mass covering the elbow joint and from light yellow to a deep yellow-brown. There is decided involvement over the articulations of the fingers. The results of physical and neurologic examinations were normal except for obesity. A sugar tolerance test gave normal results except for the one hour blood sugar value of 154 mg. per hundred cubic centimeters. The blood cholesterol amounted to 330 mg. per hundred cubic centimeters (normal figure for the laboratory is up to 200 mg).

He was given a low caloric and low cholesterol diet, and in three months he lost 8 pounds (3.5 Kg.) and was able to flex the fingers more easily. The large lesions were smaller and the small lesions showed no increase in size.

Epithelioma Adenoides Cysticum (Turban Tumor). Presented by DR. FRANCIS M. THURMON, Boston.

S. H., a 69 year old white man, has had multiple nodules on his head since birth. The first nodule appeared on the right side of the forehead, which was accidentally injured in childhood. This nodule ulcerated and has remained so since that time. No additional nodules appeared on the scalp. Approximately eight years ago several nodules were removed by a physician, and since then there has been a most rapid growth of the nodules. His mother had similar but larger nodular swellings, and she died at the age of 70. His maternal grandfather and

several maternal grandaunts had similar nodules of the sclp. There was a large verrucous mass on the back which was removed and histologically proved to be a low grade epithelioma of the sweat gland type.

Clustered on the anterior half of the scalp and encroaching on the forehead there is a large mass of lobulated lesions which vary from 1 to 5 cm. in diameter. These lesions are elevated from 3 to 5 cm. and extend laterally down to the ears. They are pale with a bluish tinge. There are slight crusting and scarring of a few of the older lesions. A few of the nodules are similar to wens. Most of them are soft, but a few are firm. All are nontender and painless.

Histologic examination revealed the nodules and masses to be composed of basal cell type of epithelium, arranged in sheets, in small closely packed clusters and in cystic configuration.

The urine showed a large trace of albumin and many casts. He received roentgen ray therapy, 500 r in a single exposure to two lesions, 20 cm. distance, 0.25 mm. of copper, 200 kilovolts, closely screened, with no effect. Surgical excision and application of Thiersch skin grafts were successful on all nodules thus removed, and electrocoagulation successfully destroyed other nodules.

DISCUSSION

DR. FRANCIS M. THURMON, Boston: This case is presented because the condition is interesting, unusual and of long duration and also to call attention to the fact that these tumors are radioresistant.

CLEVELAND DERMATOLOGICAL SOCIETY

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March 27, 1941

Discrete Keratoderma (Michael). Presented by DR. GEORGE H. CURTIS and DR. E. W. NETHERTON.

H. N. W., a white man aged 38, has had lesions on the dorsa of the hands for eight years. There have been periods of improvement and exacerbation. During the exacerbations the lesions are thickened and tend to become fissured. They have never been pruritic and are not affected by the seasons, nor do they improve when he is away from work for from a few weeks to a year at a time.

There are a number of dry brownish red and fairly well demarcated plaques on the dorsa of the hands and knuckles. They vary from 1 to 3 cm. in diameter, the smaller lesions being roughly circular and the larger ones irregular in shape. The surfaces vary from slightly scaly to mildly verrucous. The lesions on the knuckles show a tendency toward fissuring. The hemogram and the urine were normal. The blood sugar content was 97 mg. per hundred cubic centimeters. The cholesterol content of the blood was 137 mg. per hundred cubic centimeters. The Wassermann and Kahn reactions of the blood were negative.

The striking features of the biopsy sections were hyperkeratosis, acanthosis, elongated papillae and a rather dense perivascular round cell infiltration, beginning in the upper part of the corium and following along the blood vessels into the papillae. One half of the biopsy section showed a striking dense hyperkeratosis without parakeratosis situated on a thick granular cell layer, averaging about six

cells thick but varying from four to eight cells thick. The half of the section toward the central part of the lesion showed alternating verticle palisade layers of parakeratosis and hyperkeratosis. The granular cell layer immediately beneath the bands of parakeratosis was absent or very thin, seldom over two cells thick. There were no Monro abscesses. From the periphery the acanthosis became marked, with elongation of the rete pegs and papillae. In the upper part of the corium, except at the periphery, where there was little edema or cellular infiltration, almost all the papillae and the normal tissue structure were replaced by edema, rather dense round cell infiltration and fibrous tissue proliferation. At the apexes of many of the papillae the basement membrane had been disrupted. In the upper part of the corium the rather dense cellular infiltration was almost entirely perivascular and followed along the blood vessels into the papillae.

The deep part of the corium and the subcutaneous tissue appeared normal.

DISCUSSION

DR. J. E. FISHER: I saw this patient two years ago. The lesions appeared more or less as dry, scaly patches which cleared up after one or two roentgen ray treatments and the application of a mild ointment.

DR. H. J. PARKHURST, Toledo, Ohio: The clinical and histologic picture together with the lack of subjective symptoms correspond to the description given by Michael. I agree with the diagnosis as presented.

Xanthoma Tuberosum Multiplex. Presented by DR. GEORGE H. CURTIS and DR. E. W. NETHERTON.

Mrs. L. H. P., a white woman aged 39, three years ago noticed some yellow pinhead-sized nodules on the elbows. Since then yellow spots and nodules have appeared on the palms, extremities and trunk. On the elbows and palmar surfaces of the fingers some of the lesions have grown to the size of a pea. She consulted us in order to have the larger lesions removed because they were tender on pressure.

In February 1940 she had an abscess in the left external auditory meatus and received a blood transfusion. Since that time she has gained 30 pounds (13.5 Kg.) in weight.

The family history and past personal history are irrelevant.

The general physical and neurologic examinations showed a normal but obese woman. The results of an endocrinologic survey and liver function studies were normal. Roentgenograms of the chest, gallbladder, skull, kidney regions and gastrointestinal series were normal. The retinas showed no lipemic retinitis.

On the palms there are numerous pinhead-sized yellow macules. All the creases are yellow, and on some of the fingers there are several small elevated pinkish yellow nodules. The folds of the skin over the dorsa of the finger joints are yellow. On the elbows there are pinhead-sized yellow papules and nodules varying in size up to that of a pea. The larger nodules are pinkish yellow and slightly tender on pressure. On the buttocks there are aggregations of yellow papules. Scattered over the trunk and extremities are pinhead-sized yellow papules. There are one or two nodules on the toes.

The following laboratory tests gave negative results: Sugar tolerance test, liver and gallbladder function tests, gastric analysis, hemograms, urinalysis, Wassermann and Kahn tests and determinations of icterus index and uric acid content of the blood. The basal metabolic rate varied from +9 to −7 per cent. The fasting blood cholesterol content on admission was 543 mg. per hundred cubic centimeters.

Biopsies of tissue from a papular and a nodular lesion confirmed the clinical diagnosis.

The patient was hospitalized and given the following regimen: An 800 calory, low fat diet, plus vitamins and thyroid up to 2 grains (0.13 Gm.) daily. Determinations of the fasting blood cholesterol (per hundred cubic centimeters) showed the following changes:

February 11	543 mg. (admission)
February 15	516 mg.
February 18	447 mg.
February 21	416 mg.
February 24	410 mg.
February 28	357 mg.
March 31	277 mg.

During this period the diet was gradually reduced to 545 calories daily. The larger lesions show a slight but definite decrease in size, and some of the papules on the trunk have disappeared. At home she was given a low fat diet of approximately 800 calories.

DISCUSSION

DR. GEORGE H. CURTIS: We had no particular reasons to present this case except to show the effects of diet on the cholesterol content of the blood. It brought the cholesterol content down from 543 mg. to 277 mg. per hundred cubic centimeters of blood. The lesions on her elbows and the pea-sized lesions on her fingers have decreased in size. She had a number of spots on her palms, and some of those disappeared.

A Case for Diagnosis (Psoriasis Pustulosa? Acrodermatitis Perstans?).
Presented by DR. GEORGE H. CURTIS and DR. E. W. NETHERTON.

J. T. Z., an Italian woman aged 25, in the summer of 1935 noticed small red spots on the fingers accompanied by itching and burning. They slowly enlarged by peripheral extension, but the progress has been interspersed with periods of partial remission. The lesions increased in size during exacerbations accompanied by increased redness, pain and the formation of a thick scale from beneath which, at times, a limpid fluid exudes near the border. Lesions appeared on the soles and toes in 1936. The exacerbations are more severe in midsummer and midwinter. The longest periods of remission are in spring and fall, during which the scaling ceases, redness disappears, pain is much less and only atrophy and scarring remain. During the exacerbations new lesions appear in the sites of the old lesions and at their borders. The patient has been bedridden most of the time since 1936 because of pain and tenderness.

The family history is irrelevant. The patient has enjoyed good health except for the present disability. There is no history of syphilis in the immediate family. The Wassermann and Kahn reactions of the blood of the mother, sister and brother were negative. The patient is a virgin and presents no stigmas of congenital syphilis.

The eruption at present is in a stage of partial remission. The hands, i. e., the fingers and palms, are the principal sites of the lesions. The lesions are sharply demarcated and consist for the most part of atrophy and cicatrization. Within these areas there are erythematous, slightly elevated scaling macules, which may be in the central part of the area of atrophy, or smaller macules, at the borders. The lesions vary in size from 0.5 cm. in diameter to patches involving the whole of the areas over the ulnas and one half of the palms and extending distally to include almost the entire little finger. On most of the fingers lesions completely encircle the distal phalanges and extend underneath the free border of the nails. The nails are unaffected. On the dorsum of the left hand are several small superficial depigmented scars. There are a few small macules on the dorsum of the right hand near the knuckles. The soles and toes show the same process. The aching pain which has been prominent has now disappeared.

During an exacerbation, the macular lesions become more erythematous, slightly more elevated, larger and scaling. Fissures develop in some of the lesions. Exudation beneath the scaly lesions makes them soft or mushy. Pustules have been present in the lesions on various occasions.

The hemogram and the blood sugar and blood urea values were normal. Urinalyses revealed persistent faint traces of albumin. The blood sugar (fasting) content was 85 mg. per hundred cubic centimeters. The blood cholesterol (fasting) content was 147 mg. per hundred cubic centimeters. The blood urea amounted to 30 mg. per hundred cubic centimeters. Mantoux tests with tuberculin gave negative results. Aerobic and anaerobic cultures of material from lesions showed only a growth of Staphylococcus albus. Examination and culture of lesions for fungi gave negative results. Serologic tests for syphilis gave negative results.

Histologic examination revealed the following picture: The horny layer of the epidermis showed hyperkeratosis and parakeratosis with rather large abscesses composed of pyknotic cells. In some places beneath the parakeratosis the granular cell layer was absent or thin. The malpighian layer was acanthotic; but the rete pegs were irregularly elongated, and some were broad while others were relatively thin. The upper part of the corium and the papillae showed a moderate degree of edema and proliferation of the blood vessels and moderately dilated vessels. There was proliferation of the fibrous tissue and a mild diffuse round cell infiltration. In the deep part of the corium the blood vessels were surrounded by considerable fibrous tissue proliferation. Here the lumens of some of the blood vessels were occluded and the walls were edematous.

DISCUSSION

DR. J. E. FISHER: I agree with the diagnosis of psoriasis pustulosa. On the right elbow there are characteristic psoriatic lesions.

DR. R. E. BARNEY: The history states that the patient has had recurrent attacks of pustules, which she does not present at present. Because of the type of scaling shown in the lesions now, I thought of the possibility of lupus erythematosus.

DR. I. L. SCHOENBERG: The patient states that last year an eruption developed on the face involving the cheeks, which was diagnosed as lupus erythematosus.

DR. GEORGE H. CURTIS: We have hospitalized this patient for a month, and in spite of our studies we have not been able to make a definite diagnosis. We administered bismuth therapy and potassium iodide for three weeks, and she felt a lot better subjectively. We have also administered bismarsen for about three months, and she feels better now than she has in the last five years. This is the first time she has been able to walk since 1936.

A Case for Diagnosis (Persistent Nonpitting Edema of the Eyelids; Elephantiasis Due to Lymphogranuloma Venereum?). Presented by DR. GEORGE H. CURTIS and DR. E. W. NETHERTON.

Mrs. W. D. H., a white woman aged 44, one day in August 1940 noticed itching of the eyelids, and the following day they became swollen. Two days before the onset of the symptoms the patient had a black hair rinse. In February 1941 the left eyelids began to swell. At the onset of the symptoms of the right eyelids the patient was working in a florist shop; however, she had not been in the shop for a month before the onset of her trouble, nor had she had a hair rinse. The itching is a minor symptom. There have been no remissions or exacerbations.

The results of general physical and neurologic examinations were normal. Examination of the nose and throat and roentgenograms of the sinuses showed no abnormalities. Ophthalmologic examination showed patent lacrimal ducts and no disease of the orbits.

The eyelids of both eyes are swollen and edematous. The overlying skin is dusky red. The lower lids show the greatest swelling, that of the right lower lid being about the size of a bantam egg. The swelling is soft and nonpitting and completely encircles the eye; i. e., it involves the tissues just lateral and medial

to the canthi, extending medially for a short distance on the sides of the nose, as well as the lids. Although the skin is red and shiny, there is no dermatitis or scaling, and the conjunctivas and eyeballs are normal. There is no regional adenopathy.

The hemogram showed: erythrocytes, 4,250,000; hemoglobin, 82 per cent; leukocytes, 5,200, and a differential count of polymorphonuclear leukocytes 59 per cent, eosinophils 1 per cent and lymphocytes 40 per cent. The sedimentation rate was 0.23 mm. per minute. The urine was normal. The fasting blood sugar was 111 mg. per hundred cubic centimeters. Serologic tests for syphilis gave negative results. A culture of gallbladder drainage showed Staphylococcus albus, a gram-negative bacillus and a yeastlike organism. The reaction to a Frei test was positive.

Complete studies of allergy, including elimination diets, avoidance of dusts and inhalants, allergen-proof bed covers, vaccine therapy with culture of material from the gallbladder and dilute hydrochloric acid with meals, have resulted in no improvement.

DISCUSSION

DR. EMERSON GILLESPIE, Canton, Ohio: I thought this condition was chronic lymphedema resulting from a low grade lymphangitis usually due to a streptococcic infection. The surface of the skin was never particularly involved. There has been neither scaling nor itching. Although there was a positive Frei reaction, the lesion itself cannot in my opinion fit in with a diagnosis of lymphogranuloma venereum.

DR. H. J. PARKHURST, Toledo, Ohio: I felt at first that the condition might be an eruption due to phenolphthalein, but the patient gave no history of having taken any of this drug, although she may have had some in food. Her history about her experience in the Mayo Clinic led me to believe that the physicians there suspected lupus erythematosus. This should be given careful consideration.

DR. GEORGE CURTIS: When I first saw this patient only the right eye was involved. It has been only about six weeks since the left eye began to swell. She went to the Mayo Clinic, but the physicians there were unable to do anything for her. We searched for foci of infection in the sinuses, tonsils and teeth, without success. But we did perform a Frei test with mouse brain antigen, and the reaction was positive. At the Mayo Clinic a Frei test gave a positive result, but she was told that the antigen was an old one; a new one was tried, which gave a negative result.

There have been 1 or 2 cases reported in the past in which chronic edema of the eyelids was associated with a positive Frei reaction. It is also sometimes associated with swelling of the skin of the penis. We have observed several cases in which only the prepuce of the penis had been swollen and Frei tests gave positive results.

DR. E. W. NETHERTON: Dr. Curtis and I have been much interested in this case. The patient has never had any great variation in the edema. It stays permanent and elastic. There never has been any inflammatory appearance on the surface of the skin. She has had no repeated attacks of erysipelas or conjunctivitis. A biopsy would perhaps be of value, but we have been unable to get a specimen.

DR. H. N. COLE: The tissue in the region of the inner canthus is rather infiltrated, and since a blockage of lymph here could result in edema of the entire upper lids, I should like to suggest a diagnosis of Boeck's sarcoid.

Generalized Sycosis Vulgaris (Lupoid Type). Presented by DR. GEORGE H. CURTIS and DR. E. W. NETHERTON.

M. F., a white man aged 38, states that an eruption began on the upper lip fifteen years ago. The regions affected in chronologic order are: fifteen years ago, the upper lip and bearded regions; twelve years ago, the pubis; thirteen years

ago, the axillas; three years ago, the anterior aspect of the right thigh, and two years ago, the dorsa of the hands. Only the hairy regions of the body are affected, and the infection disappears only when alopecia and scarring result.

He has had a great deal of varied treatment, including roentgen and ultraviolet irradiation, strong keratolytic and epilating ointments, vaccine and foreign protein therapy.

On the hairy regions of the face, periphery of the scalp, neck, axillas, pubis, hands and forearms there are follicular pustules with areas of healing, scarring and alopecia.

DISCUSSION

DR. EMERSON GILLESPIE, Canton, Ohio: Recently, I have had a patient with this follicular pustular type of eruption who also had atopic dermatitis. Many forms of therapy were tried without any definite improvement. He was then given a course of sulfanilamide therapy with great improvement in his condition.

DR. H. N. COLE: A word of caution should be said about the use of sulfanilamide and its derivatives in the treatment of cutaneous diseases. The risks taken should make one extremely cautious. They should be used only as a last resort.

Ulerythema Acneiforme. Presented by DR. E. W. NETHERTON and DR. GEORGE H. CURTIS.

J. W. J., a Negro aged 39, states that up to puberty his face was normal but that at the time when he began to shave, dark pitted lesions began to appear at the hair follicles. Over a period of years the condition finally affected the entire bearded region of the face. It has never been inflammatory.

The bearded region shows an extensive pitted scarring, stopping abruptly at the scalp on the temples. The pitted scars are follicular and vary from the size of a pinhead to that of a lentil. They are numerous, discrete and so close together that the intervening skin appears as reticulated ridges. The pits are hyperpigmented and pierced by a hair which grows straight. The hyperpigmentation makes the bearded region appear darker than the rest of the cutaneous surface. There is no clinical evidence of inflammation. The upper lip is also affected. Below the mandible the condition disappears.

DISCUSSION

DR. I. L. SCHONBERG: I believe this patient has had folliculitis and probably pulled out a lot of hairs in the face, resulting in scarring. In cases of ulerythema acneiforme the lesions do not bear any definite relation to the hair follicles but are associated with the formation of comedos. I interpret the condition in the case presented as sycosis vulgaris with scar formation.

DR. J. A. GAMMEL: In the outpatient department of Lakeside Hospital I have seen a number of Negro patients with this disease. They all showed definite linear scars that met at angles, and they usually gave a history of ingrown hairs which they have had to pull out. I have never seen exactly the same type of scars in a white person.

DR. H. N. COLE: I asked this patient if he had a pair of tweezers. He said he did and that he pulled out hairs regularly.

DR. E. W. NETHERTON: We asked him the same thing, and he said that he was sure that although he did pull some hairs, he never had numerous ingrown hairs and they did not produce the scars. The scars appeared apparently spontaneously.

DR. H. J. MISKJIAN: If pulling out hairs could produce this type of atrophy, one would see a high incidence of this condition in women with hypertrichosis.

Trophoneurosis. Presented by Dr. E. W. Netherton and Dr. George H. Curtis.

Mrs. E. M., a white woman aged 76, during the past six years has had recurrent attacks of a red, swollen, itching and burning eruption on the right side of the face. The area is extremely sensitive to touch. At times it has been moist, but it has never been vesicular. The attacks usually subside within several days and recur at intervals of from two to six months. During the remissions, the itching and burning persist, but to a lesser degree than during the exacerbations. The last attack persisted longer than usual, having its onset on Dec. 24, 1940 and persisting to the beginning of roentgen ray therapy, about Jan. 20, 1941. The onset of this exacerbation was accompanied by severe lancinating pains in the head and on the right side of the face, nausea and vomiting. There is no history of drug ingestion.

The general physical examination showed the usual physique of a woman aged 76, with an enlarged heart, systolic murmur and arteriosclerosis. There was no evidence of infection in the sinuses or in the nasal and pharyngeal cavities.

There is a poorly defined, light red, smooth, edematous, tender plaque on the right side of the face. It is rather sharply limited at the midline of the face and extends from the right side of the nose to a vertical line at the lateral margin of the orbit and from the upper margin of the zygoma downward to the upper half of the upper lip. The lesion is dry and not vesicular.

Treatment consisted of roentgen ray therapy of high voltage to the trigeminal ganglion, resulting in a rapid subsidence of the subjective symptoms.

The hemogram was normal. Serologic tests for syphilis gave negative results. A request for a biopsy was refused by the patient.

DISCUSSION

Dr. E. W. Netherton: Intense burning has been the chief complaint of this woman. After the roentgen ray therapy her symptoms were greatly relieved. There is an associated retinitis of the right eye. The oculists at the clinic believe her symptoms can be explained on the basis of avitaminosis. She is now receiving vitamin B complex.

Kaposi's Sarcoma with Involvement of the Oropharynx and Larynx. Presented by Dr. Otto E. L. Schmidt.

A. P., an Italian laborer aged 65, presented from the department of dermatology and syphilology, Lakeside Hospital, complaints of difficult breathing for two weeks and an eruption for three years.

He has always been exceptionally healthy. Three years ago he noted a cluster of small reddish plaques in the right groin; these slowly coalesced, became purplish and formed a hard lesion about 5 by 3 cm. Two and one-half years ago his ears became thickened and nodular, and since then reddish nodules and plaques have appeared on the feet, hands, thighs, arms and chin. Two weeks prior to his entry into the hospital, on Feb. 13, 1941, he began to have attacks of paroxysmal dyspnea and hoarseness.

The ears are thick, and there are small pink nodules in their substance. On the lower lip and chin there is a red plaque, 3 by 3 cm., with several smaller nodules surrounding it. On the trunk, arms and legs there are scattered flat infiltrated reddish plaques, varying from 0.5 to 3 cm. in diameter. On the dorsa of the hands and on the distal portions of the feet there are larger (3 to 4 by 4 to 6 cm.) plaques. The initial lesion is a 4 by 8 cm. firm nodular infiltrated reddish to purplish black mass in the medial upper portion of the right thigh near the inguinal fold. Extending laterally and medially onto the perineum are reddish plaques and purplish nodules.

On the soft palate, fauces and posterior pharynx there is a rather sharply marginated purplish red raised and edematous lesion. The epiglottis is thickened

and involved by the same process, as also are the base of the tongue, piriform sinus, aryepiglottic fold, false cords and ventricular areas. The true cords could not be visualized.

The urine and the hemogram were normal. Serologic tests for syphilis gave negative results. Roentgenograms of the chest, feet, hands and a partial gastrointestinal series showed calcification of the pedal vessels, slight hypertrophic changes in the fingers and several small areas of destruction of bone in the metaphysial extremities of the middle phalanges of both middle fingers. All other structures were normal.

Biopsy specimens from lesions in the right groin, the dorsum of the left hand, the soft palate and the right aryepiglottic fold showed in various areas large foci of mononuclear cells, hemosiderin-containing phagocytes, capillary proliferation with endothelial hyperplasia, zones of recent hemorrhage, areas of compactly arranged spindle cells, new-formed vascular spaces and reticulum hyperplasia.

While the patient was in the hospital, a prophylactic tracheotomy was performed, and roentgen therapy in divided doses over a ten day period was given, as follows: the right extremities, 375 r; the left extremities, 225 r; the torso, 90 r; the right side of the face and neck, 900 r, and the left side of the face and neck, 1,100 r. After this therapy, laryngoscopy and tracheoscopy showed that the vocal cords were somewhat thickened and irregular and that there was no involvement of the subglottic or tracheal areas. Clinically there was less swelling of the visible oropharyngeal lesions. The cutaneous lesions were paler and flatter, especially on the hand. The tracheotomy tube was removed without dyspnea at the time of discharge from the hospital, on March 19, 1941.

Symmetric Hyperpigmentation of the Face. Presented by DR. H. G. MISKJIAN.

J. D., a mulatto aged 30, about six years ago noticed a faint brownish patch on the right malar region. It has gradually become darker. A little later a similar patch appeared on the left cheek. An area of the same type developed on the forehead much later. The change in the color of the skin was not preceded or associated with any redness, swelling or itching. There have been no subjective symptoms at any time. He has always been employed as an office worker and has never worked with oils or tars. He has not been taking any laxatives or other medicine internally.

At the age of 5 or 6 years he had what he calls "infantile paralysis," resulting in paralysis of both legs for four or five years. At present he has no signs of weakness in the lower limbs.

On each side of the face, about an inch (2.5 cm.) below the eye, there is a sharply defined patch of dark brown hyperpigmentation. These patches are roughly oval; the one on the right side measures 11 by 6 cm., and the one on the left is a little smaller. A little beyond the lateral limit of the right patch there is a small fainter area separated from the former by a narrow zone of normal skin. On the forehead, in the region between the eyebrows, there is a triangular patch similar to those on the cheeks, measuring 8 by 6 cm. A slight hyperpigmentation, in the form of numerous small punctate areas, can be seen on the upper lip, particularly above the corners of the mouth. The surface of the three main patches shows no trace of atrophy or inflammatory reaction.

Examination of the buccal mucosa shows nothing abnormal. The rest of the skin is normal.

The hemogram was normal. Serologic tests for syphilis gave negative results.

DISCUSSION

DR. H. N. COLE: I should make a diagnosis of chloasma.

DR. H. J. PARKHURST, Toledo, Ohio: In a mulatto pigmentation from any cause would likely be darker than in white persons.

DR. E. W. NETHERTON: While chloasma is usually seen in women, I believe this condition is an example of that disease.

DR. H. G. MISKJIAN: I presented this case because I feel that hyperpigmentations of the skin are very significant. Many cases of hyperpigmentation are observed in which one cannot establish a clinical diagnosis. In this case the pigmentation is darker than that seen in cases of chloasma.

A Case for Diagnosis (Xanthoma? Lupus Erythematosus with Xanthomatous Infiltration?). Presented by DR. E. W. NETHERTON and DR. GEORGE H. CURTIS.

S. C., a white woman aged 45, a teacher, ten years ago noticed a small red spot on the right cheek. She states that it felt as if it were "burned with steam." Three years ago a similar burning spot appeared on the left cheek and on the bridge of the nose. Other lesions have appeared since then on the cheeks. At times they seem to become inflamed and rise up "like a hive." During these episodes the burning sensation becomes more intense.

Four paternal uncles and one paternal aunt died from diabetes.

A roentgenogram of the chest was normal.

On each cheek in the region of the zygoma there is a roughly circular elevated plaque a little larger than a silver dollar. The border is raised and irregular but well demarcated and slightly erythematous. These plaques as a whole have a distinct yellow background beneath a superficial erythema. The central part of the lesions appears slightly atrophic and depressed in relation to the border but not to the normal surface of the skin. In the lesion on the right cheek the erythema is situated peripherally, while on the left cheek it takes the form of a coarse network. Where the erythema is not present the yellow color is apparent. At the superior margin of the lesion on the left cheek there is an extension near the outer canthus which shows definite follicular keratotic plugging. Otherwise, the surface of all the lesions is smooth and not scaling.

The several other smaller lesions on each side of the face vary from a dull pale red to a distinct yellow similar to the large plaques.

On diascopy, the yellow color is seen to be due to yellow deposits in the cutis.

The hemogram and the urine were normal. The blood sugar content was 106 mg. per hundred cubic centimeters. The fasting blood cholesterol content was 200 mg. per hundred cubic centimeters. The reaction to a Mantoux test with tuberculin (purified protein derivative) in the first strength was negative and with the second strength positive.

Histologic examination showed the horny layer of the epidermis to be mildly hyperkeratotic. The follicles were moderately dilated and filled with keratotic material. Where the lipoid cells were most numerous the epidermis was flattened and the rows of prickle cells were reduced from the normal of 5 to 7 cells to 3 to 4 cells. There was a sparse invasion of the epidermis with round cells and a diffuse spongiosis. There were no rete pegs or papillae.

In the upper and middle parts of the corium groups of from 4 to 10 large foam cells were scattered here and there and also aggregated, but without relation to other structures of the skin. A diffuse edema and considerable fibrous tissue proliferation had displaced much of the collagen fibers. Around the hair follicles there was localized round cell infiltration between the follicles in the upper part of the corium, but in the deep part of the corium and in the subcutaneous tissue the infiltrate became perivascular and more intense and diffuse in the fatty tissues.

Where the groups of foam cells in the upper part of the corium were aggregated there was a definite absence of dilated blood vessels, while in those places where groups of foam cells were infrequent dilated blood vessels were prominent. The groups of foam cells corresponded with the yellow spots seen on diascopy, and the dilated blood vessels corresponded with the areas of erythema in the lesions.

DISCUSSION

DR. HUGO HECHT (by invitation): This condition is a combination of lupus erythematosus and xanthoma. This case is the first instance of this type I have encountered.

DR. H. N. COLE: An article was written some ten years ago by Weidman (Weidman, F. D.: The Pathology of the Yellowing Dermatoses, ARCH. DERMAT. & SYPH. **24**:954-991 [Dec.] 1931) in which he discussed the changes taking place in certain chronic dermatoses. They may even be seen in certain of the granulomas, and I have personally seen them in syphilis. With these changes there may be a tendency for the chronic inflammatory process to take on this picture. In my estimation, this patient's condition comes under this category.

H. N. COLE, M.D., *President*

C. G. LAROCCO, M.D., *Secretary*

JAMES R. DRIVER, M.D., *Reporter*

April 24, 1941

Exfoliative Dermatitis (Lymphoblastoma?). Presented by DR. OTTO E. L. SCHMIDT.

C. C., a white man aged 53, an electric crane operator, presented from the department of dermatology and syphilology of the University Hospitals, complains of a generalized eruption of nine weeks' duration. Fifteen years ago he suffered extensive burns of the trunk and left arm but otherwise has always been well.

Ten weeks ago an itchy eruption appeared on both wrists, and subsequent to the use of local remedies it spread over the entire body. Two weeks after the onset he entered the University Hospital, at which time he exhibited a generalized erythematous papular eruption with excoriation, weeping, crusting and scaling. The liver was enlarged 1 fingerbreadth below the right costal margin. There was generalized fairly severe lymphadenopathy.

At the time of entrance to the hospital there was the slightest possible reaction for albumin and an occasional leukocyte in the urine. The erythrocyte count was 5,200,000. The hemoglobin content was 95 per cent. The leukocyte count was 7,400, with 56 per cent polymorphonuclear leukocytes, 21 per cent lymphocytes, 4 per cent monocytes and 18 per cent eosinophils. The Kline exclusion test gave a negative result. Roentgenograms of the chest showed clear pulmonary fields and a moderately dilated aorta.

Histologic examination of skin from the thigh showed acute and chronic inflammation.

During the patient's stay in the hospital local remedies, including potassium permanganate (1 : 5,000) tub baths, mild tar ointments, cold cream and roentgenotherapy, were of no avail, and the dermatitis became more intense and painful. After transfer to another ward, his temperature spiked up to 39.5 C. (103.1 F.), and his pulse became accelerated. There were occasional shaking chills, and he was emotionally disturbed. Three weeks ago the skin and subcutaneous tissue became edematous, especially on the legs and abdominal wall. The hands and arms were swollen, and the joints were painful. Coarse rales were present bilaterally, and a roentgenogram of the chest showed diffuse linear mottling, especially on the left side. His temperature rose to 40 C. (104 F.).

Two weeks ago albuminuria became more severe, and there were numerous erythrocytes, leukocytes and granular casts in the urine. Suddenly the leukocyte count dropped from 16,400 to 3,240 and the hemoglobin content from 87 to 66 per

cent. These symptoms were interpreted as indicative of bronchopneumonia. The urea nitrogen content of the blood, the fasting blood sugar and the cholesterol content of the plasma were normal, but the protein content of the plasma was reduced to 5.06 Gm. per hundred cubic centimeters, with an albumin-globulin ratio of 0.93.

A blood culture nine days ago showed Staphylococcus aureus (which did not cause fermenting of mannitol). Repeated blood cultures have shown no growth. A transfusion of 500 cc. of whole blood eight days ago was followed by general improvement in the edema, mental state and temperature. Repeated blood cultures are negative after five days' incubation.

DISCUSSION

DR. J. R. DRIVER: My associates and I have had in mind one of the lymphoblastomas, possibly Hodgkin's disease. Since the patient has been hospitalized his eruption has become worse and he has recently recovered from bronchopneumonia. Because of the presence of secondary infection of the skin, we have hesitated to take a specimen from a lymph node for biopsy. Further studies will be made.

DR. R. E. BARNEY: The possibility of lymphoblastoma is evidenced by the rapid change in the leukocyte count. I, too, felt that this case should be kept under observation for a time with the possibility that one of the lymphoblastomas might later develop.

DR. GEORGE H. CURTIS: My associates and I have recently studied a similar case. Our patient had the same type of cutaneous reaction with the exception that the dermatitis was more urticarial. The patient had several attacks of edema of the legs and feet, and there was a generalized adenopathy, particularly evidenced in the axillary and inguinal nodes. The eosinophil count was as high as 78 per cent. The temperature curve in the case presented and in our case, as I interpret, closely resemble that seen in the Pel-Ebstein syndrome and in Hodgkin's disease. Histologic examination of the skin showed some acanthosis and chronic nonspecific inflammatory reaction in the upper part of the corium with great numbers of eosinophils. The normal architecture of the lymph nodes was almost entirely displaced by eosinophilic infiltration. The general histologic picture in the lymph nodes was characteristic of Hodgkin's disease with the exception that there were no Sternberg's giant cells. Hodgkin's disease was the most likely diagnosis. I believe this is the diagnosis in Dr. Schmidt's case also.

Lupus Erythematosus Complicated by Dermatitis Medicamentosa (Gold)? Avitaminosis? Presented by DR. GEORGE M. STROUD.

E. S., a Negro aged 53, presented from the department of dermatology and syphilology of the University Hospital, came to the outpatient clinic on Oct. 28, 1940 because of an eruption on his face of six months' duration.

There is a 1 by 1 cm. lesion on the right malar eminence showing slight atrophy and dilated follicular openings. Near the left corner of the mouth there are two coalescing erythematous round lesions, 0.75 by 0.75 cm. and 1.25 by 1 cm. respectively, with crusting and follicular plugging. A diagnosis of lupus erythematosus was made, and the patient was given eight weekly intravenous injections of gold sodium thiosulfate in doses of from 5 to 40 mg.

About one week after the eighth injection there developed general malaise, sore tongue, sore mouth and an eruption on the body which did not respond to administration of brewers' yeast and nicotinic acid. He was hospitalized on Jan. 27, 1941, at which time the eruption had become generalized and consisted of small infiltrated reddish papules and plaques with superficial lichenification and scaling. The palms and soles were red, swollen, thickened, scaly and tender. The corners of the mouth were red and macerated. The tongue was red and smooth, and on the dorsal surface there were some white patches. The buccal mucosa showed similar changes.

On microscopic examination a lichenoid papule showed hyperkeratosis, hypergranulosis, irregular atrophy of the epithelium, irregular acanthosis, liquefaction necrosis of the basal layer, follicular and nonfollicular keratotic plugs and an infiltrate around the hair follicles and sweat glands. In the papillary portion of the corium there was an infiltrate of lymphocytes, monocytes and a few polymorphonuclear leukocytes. The collagenous bundles were thickened, and melanin was present in the chromatophores of the upper part of the corium.

A high caloric, high vitamin diet was instituted, and after one week his stomatitis improved but his eruption was unchanged. Treatment for avitaminosis was continued by the administration of brewers' yeast and nicotinic acid until March 12. His eruption had changed and now was a generalized horny folliculopapular eruption, also involving the scalp. There were also numerous violaceous lichenoid patches. The condition of the tongue was slightly improved, but the tongue was still smooth, tender and red. Whitish patches were also present on the tongue and buccal mucosa.

At this time the hemogram and the urine were normal. The reaction to an intradermal injection of 1:100,000 of old tuberculin was negative after forty-eight hours. The ascorbic acid level in the blood was 0.26 mg. per hundred cubic centimeters and the prothrombin time 82 per cent of normal. Biophotometric measurements were normal. Histologic examination on March 15 of a lichenoid papule on the back and on April 19 of a newly developed red plaque on the left cheek showed no essential changes.

Treatment was continued by the use of a diet low in vitamins A, B_1 and B_2, and he was given 50 micrograms of biotin (vitamin H) daily for ten days. No significant change occurred. He was then given from 2 to 3 mg. of riboflavin intravenously for ten days, resulting in softening of the lichenoid eruption, slight thinning of the follicular eruption, slight healing of the cheilitis, moderate regeneration of the papillae of the tongue, less redness of the buccal mucosa and less tenderness of the palms and soles. He was then given 5 cc. of vitamin B complex intramuscularly daily for two weeks, with slight improvement in all the previous features as well as increase in appetite and general sense of well-being, except for the cheilitis, which became slightly worse. The intravenous administration of riboflavin was then resumed, and the cheilitis again improved after three days.

DISCUSSION

DR. E. W. NETHERTON: I believe that this man has lichen planus. He has reticulated lesions on the mucous membranes of the cheeks that are compatible with that diagnosis. The lesions of the tongue could also be the result of a severe lichen planus. The extensive eruption seen on the skin is more or less characteristic of this disease. I am inclined to believe that the entire process is lichen planus, as I could find no lesions resembling lupus erythematosus. The microscopic picture was not unlike that of lichen planus.

DR. H. J. PARKHURST, Toledo, Ohio: In view of the history that there were lesions of lupus erythematosus in the first place and that this eruption developed during the course of gold therapy, I believe this condition might well be a lichen-planus-like eruption due to the administration of a gold compound.

DR. J. R. DRIVER: I agree with Dr. Parkhurst that this eruption results from the ingestion of gold. The lesions in the mouth, while not characteristic of lichen planus, nevertheless are compatible with the type of reaction seen in cases of heavy metal poisoning.

DR. GEORGE BINKLEY: The histologic picture in this case has never impressed me as being consistent with a diagnosis of lichen planus. The eruption could be explained on the basis of dissemination of the lupus erythematosus as a result of gold therapy. The consistently low leukocyte count of around 5,000 is also suggestive of this interpretation.

Lichen Striatus. Presented by DR. OTTO E. L. SCHMIDT.

D. P., a Negress aged 5 years, presented from the department of dermatology and syphilology of the University Hospitals, complains of a linear lesion on the left arm of nine months' duration. She had pneumonia at the age of 4 months but has otherwise been well. Asymptomatic white blotches were noted on the chest, and there was a streak down the left arm in July 1940. Since their first appearance, these lesions have not changed perceptibly. Except for hypertrophied tonsils the general physical examination revealed no abnormalities.

Beginning on the left side of the chest just below the clavicle and extending from the midline laterally down the biceps over the cubital space and ending in the midportion of the flexoral surface of the forearm there is a whitish linear lesion 0.5 to 3 cm. wide, composed of single and coalescent clusters of flat or slightly raised lichenoid papules and macules. There is no underlying induration. A small partially depigmented macule is present on the right breast.

Histologic examination showed slight acanthosis. The basement membrane was intact, and no pigment was present in the epidermis. In the upper and deeper portions of the cutis there were focal collections of lymphocytes. No dilated follicles or sudoriferous glands were present.

DISCUSSION

DR. GEORGE BINKLEY: I agree with the diagnosis of lichen striatus.

DR. E. W. NETHERTON: This condition seems to be like the entity described recently by Senear and Caro (Senear, F. E., and Caro, M. R.: Lichen Striatus, ARCH. DERMAT. & SYPH. **43**:116-133 [Jan.] 1941).

A Case for Diagnosis (Lichen Nitidus? Lichen Scrofulosorum?). Presented by DR. OTTO E. L. SCHMIDT.

L. G., a Negro aged 6 years, presented from the department of dermatology and syphilology of the University Hospitals, has had a generalized eruption for eight months.

His father and an aunt died of pulmonary tuberculosis. In 1939, a tuberculin test (with a 1:10 solution) gave a negative reaction, and roentgenograms of the chest showed increased linear and softly mottled shadows extending from both hili.

He is fairly well developed and well nourished. There is a slight generalized lymphadenopathy. Physical examination of the lungs showed no abnormalities. There is an almost universally distributed eruption, sparing the lower half of the legs, popliteal spaces, palms and soles. It consists of almost uniformly sized (0.75 to 1 mm.), discrete, flat-domed, round and polygonal, flesh-colored papules, some slightly umbilicated. There is some tendency to ill defined grouping of the lesions.

The hemogram showed 82 per cent hemoglobin, 4,510,000 erythrocytes and 3,150 leukocytes, with 48 per cent polymorphonuclear leukocytes, 41 per cent lymphocytes, 9 per cent monocytes and 2 per cent eosinophils. The reaction to a tuberculin test (with a 1:1,000 solution) was negative. Roentgenograms of the chest made recently showed no evidence of infiltration in the pulmonary fields and no evidence of enlarged mediastinal nodes. Histologic examination of skin removed from the abdomen showed only mild chronic inflammation of the cutis.

There has been no change in the eruption following the administration of large doses of cod liver oil during the past four months.

Lichen Scrofulosorum. Presented by DR. OTTO E. L. SCHMIDT.

L. W., a Negress aged 17, presented from the department of dermatology and syphilology of the University Hospitals, complains of an asymptomatic eruption on her trunk for one month.

One stepbrother is a patient at Sunny Acres, Cleveland, Tuberculosis Sanatorium, Warrensville, Ohio. The patient has frequent colds with concomitant pains in the chest, cough and raising of sputum. She has accompanying night sweats and has been persistently underweight.

Examination of the skin reveals numerous small flesh-colored papules, some follicular and many extrafollicular, distributed on the lower part of the trunk anteriorly and posteriorly and on the upper portion of the buttocks. A few similar lesions are present on the arms. A moderate generalized lymphadenopathy is present.

In 1935, an intradermal tuberculin test (with a 1:10 solution) gave a negative result, and roentgenograms of the chest were normal. Roentgenograms of the chest made recently showed bilateral enlarged hilar lymph nodes. The hemogram showed 64 per cent hemoglobin, 3,590,000 erythrocytes and 4,800 leukocytes, with 57 per cent polymorphonuclear leukocytes, 32 per cent lymphocytes, 8 per cent monocytes and 3 per cent eosinophils. A tuberculin test (with a 1:25,000 solution) in forty-eight hours resulted in a 1.5 cm. bulla and a 5 cm. zone of surrounding erythema. Permission for a biopsy was refused.

DISCUSSION OF TWO CASES OF LICHEN SCROFULOSORUM

DR. GEORGE H. CURTIS: In the case of L. G., I should favor a diagnosis of lichen nitidus, because the lesions are generalized, uniform in size, flat, shiny, smooth and superficial and on close examination the surface is somewhat lighter in color than the normal skin. They have no real base, but the angulation of the lesions themselves is due to the normal markings of the skin. The whole eruption is nonscaly. Their location would seem to be interfollicular rather than follicular.

By contrast, the lesions of L. W. are larger, scaly, follicular and grouped. The lesions appear to be deeper, involving the corium. In addition, the clinical evidence of tuberculosis make the diagnosis of lichen scrofulosorum unquestionable.

Dermatitis Nodularis Necrotica. Presented by DR. FRANK M. MCDONALD, Akron, Ohio.

E. S., a white man aged 30, was first seen on March 18, 1941, complaining of pruritus of the legs for ten days, followed in five days by lesions that were thought to be "hives." Three days later, the right leg became swollen and tender, and a tender lump appeared in the right groin. There had been no previous cutaneous disease at any time. There had been no ingestion of drugs.

On examination there is a cellulitis of the right leg with right femoral lymphadenitis. In addition, there are firm pinkish papules and nodules, ranging from 1 to 4 mm. in diameter, distributed on the legs, thighs, arms and forearms. Those on the upper extremities are especially prominent in the region of the elbows. The lesions on the lower extremities are slightly tender and more inflammatory. Some appear to be excoriated, and a few are somewhat ecchymotic. In general the patient is moderately toxic. There is inflammation of the membranes of the nasal passages and of the throat of moderate severity. On examination of the heart, a slapping first sound is heard at the apex.

The urine was normal. The hemoglobin and erythrocyte count were within normal limits. There were 14,770 leukocytes, and the differential count was normal. The blood platelets numbered 240,000. The bleeding and clotting times were normal. Serologic tests for syphilis gave negative results. The sedimentation rate was increased. A roentgenogram of the chest was normal. The intracutaneous injection of 0.1 cc. of a 1:100,000 dilution of old tuberculin (Koch) elicited a negative reaction after forty-eight hours. The result of a dextrose tolerance test was normal. Blood cultures on two occasions have shown no growth.

Treatment has consisted of bed rest, adequate fluids, salicylates by mouth, hot magnesium sulfate compresses, calamine lotion, 3 per cent ammoniated mercury ointment, mercury bichloride compresses, 10 per cent bismuth tribromphenate ointment and intramuscular injections of calcium gluconate. The condition has changed its appearance considerably. The generalized intoxication disappeared within nine days. The papules on the upper extremities disappeared after two weeks. The papules and nodules on the lower extremities became progressively more ecchymotic, ecthymatous and necrotic. Mild ecchymoses also appeared over the right femoral lymph nodes. The area of cellulitis on the right leg now shows a well defined,

oval, palm-sized, bluish black adherent crust. The improvement has continued in the past two weeks, but it has been slow.

DISCUSSION

DR. B. F. BARNEY, Columbus, Ohio: I offer the diagnosis of dermatitis factitia.

DR. R. E. BARNEY: The lesions on the lower part of the abdomen and on the legs had crusts which looked as though they might have been produced by the application of a caustic.

DR. HUGO HECHT (by invitation): It is my opinion that the condition is dermatitis factitia. I was formerly in the Russian army, and many cases of this kind came to my attention. The lesions appear to be caused by the application of phenol.

DR. J. R. DRIVER: Two years ago my associates and I observed a patient at the Cleveland City Hospital with a similar condition. On the right leg there was a palm-sized lesion with a large slough, which we interpreted as resulting from an embolus. Under the title "Dermatitis Nodularis Necrotica" Duemling reported some cases of this type resulting from emboli (Duemling, W. W.: ARCH. DERMAT. & SYPH. **21**:229-250 [Feb.] 1930; **33**:99-108 [Jan.] 1936). I agree with the diagnosis as presented.

Lupus Vulgaris. Presented by DR. FRANK M. MCDONALD, Akron, Ohio.

K. V., a white woman aged 62, was first seen in the dermatologic clinic of Akron City Hospital in March 1941. The patient was born in Hungary and lived there for twenty-nine years. When she was 17 years of age, during a severe attack of whooping cough, a small papule appeared in the center of the forehead at the scalp line. The lesion was asymptomatic but persisted and slowly enlarged. About twenty years after its appearance it was the size of a 25 cent piece. At this stage a considerable loss of hair was beginning to appear. During the past fifteen years the lesion has progressed rapidly and loss of hair has been great. In the past two years the condition has apparently been stationary. A similar lesion appeared on the left wrist twenty-five years ago and has slowly enlarged.

The central portion of the forehead and the parietal areas of the scalp exhibit a dull reddish, violaceous, sharply defined, arciform, boggy lesion, measuring 13 cm. from the lower border to the uppermost edge on the scalp and 15 cm. across the forehead. The areas adjacent to the sides and upper portions show numerous macules and papules, averaging 1 cm. in diameter. They present a characteristic apple jelly color on diascopic examination.

The hair remaining on the scalp is diffusely thinned, and the skin is atrophic. Several small yellowish red macules are seen in the temporal areas. In addition, there are diffuse redness and edema of the right ear and to a lesser extent of the left ear. The dorsum of the left wrist shows a yellowish red scaling atrophic and scarring plaque 3 by 2 cm. in diameter.

The urine and the hemogram were normal. The intracutaneous injection of 0.1 cc. of a 1:10,000 dilution of old tuberculin (Koch) elicited a strongly positive reaction. Roentgenograms of the chest showed chronic bronchial changes in both pulmonary fields, probably from a tuberculous infection now quiescent.

Histologic examination showed a subepithelial mass of a granulomatous character in which there were discrete and confluent epithelioid tubercles with multinuclear giant cells separated by vascular pyogenic granulation tissue with masses of lymphocytes. There are no regions of caseation necrosis. The morphologic changes resemble those of a mixed tuberculous and pyogenic inflammation somewhat more than they do those of Boeck's sarcoid or tuberculid.

DISCUSSION

DR. H. J. PARKHURST, Toledo, Ohio: I agree with the diagnosis as far as the lesion on the forehead is concerned, but the condition of the scalp would lead one to suspect that possibly the patient might have had favus years ago. She was born in Europe in a section where favus was prevalent.

NEW ENGLAND DERMATOLOGICAL SOCIETY

JOHN G. DOWNING, M.D., *President*

FRANCIS M. THURMON, M.D., *Secretary*

Boston, April 30, 1941

Dermatitis Herpetiformis. Presented by DR. JOHN G. DOWNING, Boston.

C. J., a 22 year old man, has suffered from recurrent attacks of general malaise, itching and an eruption of the skin for three years. Various diagnoses have been made. The present attack is of three weeks' duration.

Physical examination shows a multiform symmetric eruption predominantly vesicular, with a tendency toward grouping on the scalp, face, scapulas, sacrum, flanks and arms. There is considerable pigmentation at the site of former lesions.

DISCUSSION

DR. JACOB H. SWARTZ, Boston: I think small maintaining doses of sulfanilamide or sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) are of value in cases of this kind. They do not cure, but they do check the condition, and they can be safely administered for a long period.

DR. JOHN G. DOWNING, Boston: I understand that as soon as the administration of sulfanilamide is stopped the eruption recurs.

DR. FRANCIS M. THURMON, Boston: The use of sulfanilamide in the treatment of dermatitis herpetiformis originated at the Massachusetts General Hospital. The results are temporary, lasting only as long as the drug is given. In a few cases in which the condition temporarily cleared there was a recurrence of lesions as soon as administration of the drug was stopped. I should like to suggest another form of therapy, that is, indirect roentgenotherapy over the spinal portion of the sympathetic nervous system.

Mycosis Fungoides. Presented by DR. BERNARD APPEL, Boston.

Six years ago S. N., a 64 year old man, had an eruption on the right thigh. After two years it involved the entire body. At a hospital a diagnosis of lichen planus was made, and he received about twenty injections of mercury salicylarsenate without much benefit. At a different hospital, where he stayed from May 1939 until December 1940, a diagnosis of leukaemia cutis was made, and a microscopic examination of the skin revealed nothing specific in regard to leukaemia cutis or mycosis fungoides.

The patient presents a generalized erythroderma with lichenification and scattered hyperpigmented areas with excoriations. There is generalized adenopathy.

His leukocyte count varied from 9,000 to 32,000 and the erythrocyte count averaged about 4,500,000 per cubic millimeter. A roentgen ray examination of the lungs showed hilar adenopathy. Later his blood count showed 4,700,000 erythrocytes and 25,000 leukocytes per cubic millimeter. A microscopic examination of the skin showed moderate parakeratosis and acanthosis with increased infiltrate throughout the upper layers of the cutis, the rete pegs and the epidermis of lymphocytes, plasma cells, mast cells and giant cells. He has received roentgen therapy recently. At present he is taking a proprietary mixture of fish liver oils (navitol), 120 drops per day.

DISCUSSION

DR. JACOB H. SWARTZ, Boston: I suggest a diagnosis of leukemia instead of mycosis fungoides. There is a white blood cell count of 25,000 per cubic millimeter, and the differential count shows the polymorphonuclear cells as low as 39 per cent and the large lymphocytes 40 to 50 per cent. I suggest that another biopsy be made of a gland other than the inguinal gland.

DR. C. GUY LANE, Boston: There is no doubt about the diagnosis clinically, but there is a more definite picture of the disease than this case presents. The generalized eruption with pigmentation fits into the clinical picture of a leukemic condition perfectly well, as Dr. Swartz has mentioned. It is of interest to note this man's age and the history of several years' duration. He was much older than the average patient at onset of the condition.

Mycosis Fungoides. Presented by DR. AUSTIN W. CHEEVER, Boston.

E. V., a 71 year old white man, has had a generalized eruption for about three years. The condition started on the lower extremities as small black crusts and soon spread and involved the trunk, upper extremities, face, neck and head. He was treated with various agents, including roentgen rays, sulfur ointment and home remedies. He was admitted to the Waltham Hospital for treatment of intestinal obstruction, and psoriatic-appearing lesions were noticed on the legs at the time.

A microscopic picture was consistent with mycosis fungoides. He has had diluted solution of sodium hypochlorite U. S. P. applied to the lesions in 50 per cent concentration. The surrounding tissue was protected with zinc oxide ointment.

DISCUSSION

DR. AUSTIN W. CHEEVER, Boston: I was interested in this case because there have been lesions which suggested mycosis fungoides. When I saw the patient first at the Waltham Hospital, he had seborrheic dermatitis, largely across the chest and arms, of the plaquelike type. Dr. Edward Lafreniere, who saw him before I did, said he had dermatitis to a striking extent and that the condition changed rapidly.

Twisted Hair (Pili Torti). Presented by DR. F. RONCHESE, Providence, R. I.

A. B., a 17 year old girl, was first seen in 1930 and was presented at the meeting of the New England Dermatological Society on Oct. 14, 1931 (ARCH. DERMAT. & SYPH. **25**:586 [March] 1932). The case was later published (ARCH. DERMAT. & SYPH. **26**:98 [July] 1932) under the title "Twisted Hair (Pili Torti)." The patient was seen from time to time, and the condition of her hair has improved considerably. However, it is still dry and shows twists visible to the naked eye, but it breaks off at a longer distance from the scalp than it did ten years ago. The eyebrows have remained scanty and twisted. The marked keratosis pilaris of her legs is as evident as before.

Under the microscope the hair shows the same twisting broomlike ends and splitting of the hair into two ribbon-like twisted halves.

The patient has oiled her scalp, mostly with hydrous wool fat, and has taken plain cod liver oil for a long time. The internal and external treatment, reducing the brittleness of the hair, may account for the improvement in the length of the hair, permitting a feminine hair dressing not unlike ones usually seen.

(Photographs taken ten years ago were submitted for comparison.)

DISCUSSION

DR. JOHN G. DOWNING, Boston: It is interesting to observe again this case which was presented in 1931. It was among the first of this abnormality of the hair reported in the literature. It is interesting to see how much this girl has improved.

DR. BERNARD APPEL, Boston: This congenital and hereditary anomalous condition of the hair is interesting. The improved cosmetic appearance with the passage of time in this particular instance is encouraging and should be kept in mind when one expresses an opinion of the prognosis. In my opinion the ingestion of cod liver oil played no part in the improved appearance, because the twisting of the shaft is produced by a structural condition of the hair follicles. There is no evidence that the ingestion of cod liver oil can affect the shape and

curl or twist of hair. The fact should be recognized that Dr. Ronchese was the first to call attention to this condition, by this name.

DR. FRANCIS M. THURMON, Boston: There is an excellent account of pili torti in Lee McCarthy's textbook, Diagnosis and Treatment of Diseases of the Hair (St. Louis, C. V. Mosby Company, 1940, p. 197). The case which Dr. Ronchese has presented today is cited extensively. Interesting is the fact that the scalp hairs of this patient did not clear with puberty.

Leukoplakia of the Tongue. Presented by DR. F. RONCHESE, Providence, R. I.

Since the age of 2 years, M. C., now a 12 year old girl, has had white patches on the tongue. She also has had malformation of three finger nails for ten years. Recently acne of the face, seborrhea of the scalp and cheilitis (perlèche) developed. The cheilitis soon disappeared under treatment with riboflavin given by mouth. She has not menstruated yet.

There are white areas on the tongue. Some are smooth, and some are verrucous. They involve the tongue, the inside of the cheeks and the vermilion border of the lips.

A microscopic examination showed hyperkeratosis with acanthosis and cellular reaction. Scrapings and cultures taken one year ago and repeatedly of late were negative for Monilia and other fungi.

DISCUSSION

DR. G. MARSHALL CRAWFORD, Boston: The first thought that came to mind was pachyonychia congenita. I can think of no other condition in which lesions of the mouth and of the nails appear as part of the same picture. There are some features missing, however, such as changes in the scalp and thickened plaques on the skin. The family history obtained on questioning was irrelevant.

DR. JOHN G. DOWNING, Boston: I suggest repeating mycologic studies in this case. The lesions of the oral cavity and nails resemble changes in a case I reported (Cutaneous Moniliasis Associated with Oral Thrush, ARCH. DERMAT. & SYPH. **31**:636-643 [May] 1935).

DR. FRANCIS M. THURMON, Boston: The onset of oral leukoplakia at the age of 2 years, changes in the nails, facial acne, seborrhea of the scalp and cheilitis are indicative of an avitaminosis, possibly of members of the vitamin B complex, rather than of a leukokeratosis due to oral irritation. The possibility of an avitaminosis is further substantiated by the rapid clearing of the cheilitis under treatment with riboflavin. It is generally accepted that polyvitamin therapy, especially with vitamin B complex, is of greater value than the administration of a single factor of the vitamin B complex. It would be interesting to observe the effect of a mild alkaline wash locally, the oral administration of vitamin B complex and the intramuscular injection of concentrated solution of liver extract.

Dermatitis Medicamentosa (Phenolphthalein). Presented by DR. WILLIAM P. BOARDMAN, Boston.

J. C., a 67 year old white woman, has had an eruption on her body for only a few weeks. She states that she had been taking "ex-lax" prior to the appearance of the eruption.

There are large pigmented areas on the extremities and the trunk. On some of the lesions large flaccid bullae appeared. The lesions subsided a few days later.

She was given a test dose of ¼ grain (0.016 Gm.) of phenolphthalein, and within twenty-four hours the original lesions became erythematous and bullae appeared. The lesions subsided within a few days, leaving pigmented areas.

DISCUSSION

DR. C. GUY LANE, Boston: I should like to ask the presenter if he has any information as to what caused the sharp lines of demarcation on the arms. The

eruption ends abruptly, and I wonder whether there have been any applications or dressings which might have ended at this site or whether the sleeves worn in the summer ended there.

DR. WILLIAM P. BOARDMAN, Boston: I have no explanation.

A Case for Diagnosis (Pseudo Xanthoma Elasticum?). Presented by DR. MILDRED RYAN, Brockton, Mass.

An 18 year old youth had transverse ridges across the back which were asymptomatic and were noticed by friends.

On the lower part of the thorax and in the lumbar region are striae 3 inches (8 cm.) in length and longer, running horizontally. These striae are about 1/16 and 1/4 inches (0.16 and 0.64 cm.) wide. In the thoracic region the striae are reddish purple, and in the lumbar region they are white.

DISCUSSION

DR. E. LAWRENCE OLIVER, Boston: I thought there was a possibility that the patient might have had a beating. These atrophic lesions might be the result of a beating with a whiplash.

DR. WALTER GARFIELD, Boston: Is there any history of injury?

DR. BERNARD APPEL, Boston: I think these are not lineae striae distensae, because they are not areas of atrophy but areas of hypertrophy. In my opinion this case shows the result of a pathologic change with an increase in connective and elastic tissue rather than a breaking down.

DR. FRANK B. COLLOTEN, Boston: I observed a similar picture in a 28 year old man who said that he had had the condition since early childhood and without known cause.

DR. MAURICE M. TOLMAN, Boston: The lesions have come on gradually with no history of trauma. They appear to be elevated; they have a yellowish tinge and run in a continuous line. I believe that they are due not to a breaking down but to an increase of the elastic tissue elements. I suggest a diagnosis of pseudoxanthoma elasticum.

Deficiency of Vitamins C and B. Presented by DR. WALTER T. GARFIELD, Boston.

G. S., a 56 year old man, entered the Thorndike medical service at the Boston City Hospital with a complaint of weakness and fatigue. He had been unemployed for the past one and a half years and had been forced to reduce his expenditures to 30 to 40 cents a day for food. His breakfast usually consisted of a quarter of a cup of milk, oatmeal, black coffee, 2 teaspoonfuls of sugar and one or two doughnuts. His supper consisted of a ham sandwich, a cup of coffee, 2 teaspoonfuls of sugar and a small piece of apple pie. He usually had no dinner.

Three months ago he noticed fatigue, sleeplessness and irritability. About ten days ago he began to notice palpitation of his heart and soreness of the muscles. Ten days ago he noticed a purplish discoloration on the thighs, which has spread.

There is a "sharkskin" appearance of the nose, a few carious teeth with a large amount of tartar, hyperplasia of the gums with edema and a dusky red, purplish coloration. The skin shows purplish discoloration involving the thighs in a saddle distribution. There are scattered perifollicular hemorrhages and keratosis. The backs of the hands show increased pigmentation.

His hemoglobin content was 34 per cent; the erythrocytes numbered 1,620,000 and the leukocytes 2,500 per cubic millimeter. The differential count showed 68 per cent polymorphonuclear leukocytes, 6 per cent myelocytes, 24 per cent lymphocytes and 2 per cent monocytes, with central achromia of the red blood cells and a reduction of the number of platelets.

DISCUSSION

DR. WALTER T. GARFIELD, Boston: The interesting feature in this case is the short duration of the symptoms, namely, two weeks. Apparently the patient felt all right up to that time. He was walking down the street and had a sudden weakness. He had to have help to get home, and when he did get home the inner aspects of the thighs were ecchymosed and he was very weak. He came into the hospital, and the condition was diagnosed as vitamin C and vitamin B deficiency. His tongue showed no change, and he did not complain of any soreness of the mouth. Ecchymoses occurred while he was out walking.

Syphilis Acquired at the Age of Four Years; Gumma of the Palate. Presented by DR. WALTER GARFIELD, Boston.

In September 1931 R. C., the father of this 13 year old boy, had a condition diagnosed as primary and secondary syphilis. At this time the patient's mother had a negative Kahn serologic reaction. In November 1931 the mother presented herself at the clinic with a maculopapular eruption. A Kahn reaction of the blood was positive at this time, and a diagnosis of secondary syphilis was made. In December 1931 the patient, who was then 4 years old, entered the dermatologic clinic with a macular eruption on the body and excoriations and swelling about the nasal openings. Kahn and Wassermann reactions of the blood were positive, and a diagnosis of acquired syphilis was made. The patient was given antisyphilitic therapy and received twenty-three intravenous injections of sulfarsphenamine. He then was not seen for nine years and returned to the clinic in March 1941 with a history of recurrent attacks of tonsillitis and a lesion in the throat which had been present for about one month.

There is an irregular ulceration with a surrounding erythema involving the left side of the soft palate and a portion of the uvula. There is a bilateral cervical adenopathy. A Hinton test of the blood showed a positive reaction, and antisyphilitic treatment has again been started.

DISCUSSION

DR. FRANCIS M. THURMON, Boston: This case is of interest because syphilis was innocently acquired at the early age of 4 years. Then, at the age of 13 years a destructive tertiary lesion of the soft palate and uvula developed. This case illustrates the tragedy of inadequate therapy and the fallacy of relying on the prolonged use of a single drug.

Pemphigus Foliaceus. Presented by DR. JOHN G. DOWNING, Boston.

J. F., a 49 year old man, had an eruption on his face which developed about eight months ago. At that time he visited a private physician and received local therapy. The eruption spread to other parts of the body and was characterized by blisters. The patient entered the hospital in the middle of March with a generalized eruption. There is no history of internal or parenteral medication.

He presents a picture of generalized dermatitis exfoliativa with foul-smelling greasy scales and a few bullae.

His hemoglobin content was 80 per cent; his erythrocyte count was 3,870,000, and his leukocyte count was 1,200 per cubic millimeter. The differential count showed 8 per cent eosinophils. The chemical examination of the blood showed nonprotein nitrogen 30 mg. and phosphatase 1.7 mg. per hundred cubic centimeters.

He has received starch baths, applications of antiseptic oil and vitamin D, 50,000 U. S. P. units daily, resulting in slight improvement.

DISCUSSION

DR. C. GUY LANE, Boston: At the Massachusetts General Hospital two procedures have been used. In cases of the acute type of this condition with

alteration of the acid-base balance of the blood with low sodium content, treatment with adrenal cortex extract and saline solution has produced a few good results. In other cases large doses of viosterol or similar vitamin compounds have been given.

DR. WILLIAM P. BOARDMAN, Boston: I have used this type of treatment but have not had much result from it. The patients have been given all the vitamins they could stand.

DR. BERNARD APPEL, Boston: At the Boston City Hospital I recently treated several patients with high doses of viosterol and similar preparations, and the results were uniformly disappointing.

Kaposi's Sarcoma. Presented by DR. JOHN G. DOWNING, Boston.

This 70 year old man gives an indefinite history of having a lesion on his nose and forehead for several years. He was treated at the Massachusetts General Hospital in 1937 with a diagnosis of epithelioma of the basal cell type, with a question of sarcoid of the forehead and keratosis senilis. Roentgen ray therapy was instituted.

He shows pigmented keratotic lesions of the left temporal area, about the alae nasi and of the soft palate. These lesions are multiple, raised and dark violaceous.

A microscopic examination of the tissue was consistent with Kaposi's sarcoma. He has received roentgen ray therapy with improvement.

DISCUSSION

DR. JACOB H. SWARTZ, Boston: I should like to point out that Dr. Downing and I saw lesions of the mucous membrane of the mouth. This case is similar to one which Dr. Lane and I observed, that of a person of the same age who first showed a lesion on the nose, diagnosed as melanoma but on pathologic examination consistent with Kaposi's sarcoma. There also were lesions on the buccal mucous membrane. I recall another case I observed five or six years ago in which the lesions were milder but in which there were lesions in the mouth.

Annular Papular Syphilid. Presented by DR. WILLIAM WOLF, Lowell, Mass.

E. R., a 35 year old negress, married, complains of an eruption which has been present on the body for about three weeks.

Examination shows an eruption involving the flexor surfaces of the arms, abdominal area and neck. The lesions are annular with darkened pigmented central areas and more lightly colored, raised, papular borders. The mucous membranes are normal.

Hinton, Kahn and Wassermann reactions of the blood were positive. She is being given antisyphilitic therapy.

DISCUSSION

DR. J. HARPER BLAISDELL, Boston: When I first looked at the patient, my diagnosis was not syphilis, in spite of the fact that she has a positive Hinton or Wassermann reaction of the blood. If the disease is syphilis, it is remarkable that there should be no lesions on the palms or soles and that there never have been. There is one other thing to be taken into consideration: She has been in the habit of taking "feen-a-mint" once a week.

DR. GEORGE DIX, Worcester, Mass.: This woman shows a rather varied picture, but syphilis can simulate or complicate the clinical picture of any other cutaneous disease. On the front of the wrist she shows an area suggestive of lichen planus, and she says that it itched at one time. I think it is unusual to see that type of pigmentation in syphilis, especially limited to the centers of the lesions. She states that she has had no oral or palmar lesions.

DR. WILLIAM E. LONG (by invitation), Boston: I had the opportunity to see this patient the day she was admitted to the clinic. At that time she presented typical secondary syphilis. The lesions were annular and had a definite elevated palpable border. The lesions on the neck and around the hair line were typical of this type of syphilis in the Negro race. The characteristics of these lesions have now cleared, as a result of treatment. In regard to the question of pigmentation in Negro skin, I should like to say that this follows a variety of conditions and may persist for long periods, with no adequate explanation. The question today is "What was it?", not "What is it?" If one had seen the patient when she first presented herself, one would have seen an entirely different picture than is presented today. These lesions were characteristic and were typical annular lesions. There is a faint arciform pigmented line just above the left angle of the mouth which was elevated and papular. Lesions of the mucous membranes may be seen with no lesions of the skin; likewise the reverse is true. Lesions may be present on the soles with none present on the palms, skin or mucous membranes. These are the variations for which one must ever be alert.

Purpura Annularis Telangiectodes. Presented by DR. F. RONCHESE, Providence, R. I.

N. P., a 22 year old man, has had an eruption on his arms and legs for one and one-half years. There is no itching, and he has always been in good health.

There are numerous round, annular patches with slight scaling and definite wrinkling. The color varies from bright red to deep brownish red to brown. The brown discoloration corresponds to the stage of involution of the eruption and is seen mostly in the center of the patch. The red areas are telangiectatic, atrophic and purpuric. There is no atrophy in the brown area.

The basal metabolic rate was —5 per cent. His hemoglobin content was 108 per cent, and the erythrocyte count was 5,375,000 per cubic millimeter. Chemical examination of the blood showed the following results: urea nitrogen, 14 mg. per hundred cubic centimeters; sugar, 50 mg., and cholesterol, 172 mg. The coagulation time was five minutes, and the bleeding time was one minute. The reaction to a tuberculin test with a 1:1,000 dilution of old tuberculin was positive. The tourniquet test gave a negative reaction. Scrapings and cultures were negative for fungi.

The histologic examination by Drs. Satenstein and Sachs, New York, was reported as follows: "The process is in the upper part of the cutis. There are small somewhat dilated vessels of the same size and shape and arranged in groups (telangiectases). About these is a moderate cellular infiltration, with some interstitial edema. The overlying epidermis shows no noteworthy changes. The vessel walls are thickened and somewhat shiny, but there is no definite hyaline degeneration. The cellular infiltration is composed of small round cells and some wandering connective tissue cells. There is considerable hemorrhage present. The Perl stain (iron) is positive. The diagnosis is purpura annularis telangiectodes (Majocchi's disease)."

Lupus Vulgaris Erythematodes (Leloir). Presented by DR. F. RONCHESE, Providence, R. I.

G. T., a white man, has had an eruption on the right side of the face, neck, upper part of the chest and back for about thirty years. A few nodular lesions developed on the neck about thirty years ago, and the eruption spread over the presently involved areas four years ago.

There is a scaly erythematopapular eruption on the neck, ears, right side of the face and upper parts of the neck and shoulders. There is no pain or itching of the lesions. The reaction to a tuberculin test with a 1:1,000 dilution of old

tuberculin was positive. The microscopic examination of the tissue showed typical hypertrophy of the epidermis, infiltration of the cutis and giant cells, as in tuberculosis of the skin.

DISCUSSION

DR. F. RONCHESE, Providence, R. I.: This type of lupus vulgaris seems to be as resistant as the more common nodular type. It commonly resembles lupus erythematosus so closely as to be mistaken for it unless studied carefully. It represents the progressing, spreading, cutaneous type of tuberculosis of the skin which starts early in life as a primary involvement. I suggest treatment with chaulmoogra oil esters, both intramuscularly for the general effect and into the affected areas in small doses for the local effect.